The neuropsychology of visual imagery and visual hallucinations : fMRI and clinical studies.

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The Neuropsychology of Visual Imagery and Visual Hallucinations: fMRI and Clinical Studies

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ABSTRACT

Visual hallucinations are a common symptom of neuropsychiatric disorders. It is estimated that up to 33% of Parkinson's patients undergoing long-term treatment will have visual hallucinations (VHs) during the course of their illness. Although the neural and cognitive mechanisms underlying visual hallucinations largely remain a mystery, the ability of the human visual system to interpret "imaginal" and "external" events is essential if confusion between the two is to be avoided. The aims of this thesis were two fold: first to explore the "imaginal" and "perceptual" systems of normal subjects, and second, to examine the phenomenology and neuropsychology of visual hallucination in patients with Parkinson's disease (PD). A symptom-based approach was taken and it was proposed that abnormally vivid mental imagery together with impaired perceptual processing would be the link between visual hallucinations and Parkinson's disease.

This thesis begins by examining visual imagery using functional magnetic resonance imaging (fMRI) to observe brain activation while normal subjects are performing comparable imagery and perception tasks. Three experiments are reported to elucidate these processes. The studies involved comparing brain activations of perceptual, imaginal and illusory stimuli. Briefly, these experiments identified the functional roles played by different regions of the brain in “experiencing" visual stimuli from both external and internal sources. Comparison of these brain regions revealed the functional process underlying imagery and perception and possible sites of convergence and differentiation between the two experiences, imagery and perception.

In section two, a questionnaire study elicited reports of the hallucinatory experience in P.D patients and the key features of this phenomenon are discussed. Visual hallucinations in PD seem to be the result of a complex interaction of many components, including cognitive, perceptual and environmental factors. The final study revealed that compared with non-hallucinating PD patients and age-matched controls, hallucinating PD patients have difficulty in identifying impoverished or degraded objects. Hallucinators also have difficulty in judging whether an item has been imagined or perceived, and problems "recalling" the recollective experience of the encoding event. These finding are discussed and a theory on the aetiology of visual hallucinations in PD offered.

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SECTION 1: PERCEPTION, IMAGERY AND HALLUCINATIONS

Chapter 1:Introduction and Experimental Methods

1.1 Introduction

1.1.1 The imagery debate

The study of visual processing has been going on for over a century and has arguably been one of experimental psychology's most successful areas of exploration. Over this time, and using various methodologies, important information about the processes behind normal human vision have been discovered. Today, we have a considerable understanding of the neurophysiology of vision both at a cellular level in the retina and at the modular level in the occipital cortex. Cells in certain areas of the occipital cortex selectively respond to particular stimulus properties, such as motion or colour. Great advances have been made in the area of low-level vision, where the processing is driven by the stimulus, and processing is implicitly coupled with the properties of the stimulus being viewed. However, the brain also represents objects and scenes without there being any retinal input. This process relies on previously stored information about events and objects in the world. Information can then be manipulated in the "mind's eye". This thesis will examine some of the processes underlying visual mental imagery, which over the past three decades has become a major topic of scientific study.

Visual mental imagery has been the subject of much controversy and the subject of many debates. Whether this cognitive process is subserved by the same neural substrate as visual perception is one of the major controversies in visual neuroscience (Roland & Gulyas, 1994; Kosslyn & Oschsner, 1994). A variety of studies have

investigated the idea that imagery is a "top down" activation of perceptual representations. To support this, psychologists such as Kosslyn (1980) have devised ingenious experimental paradigms in which imagery and perception can be compared. In terms of their behavioural response, imagery and perception have many similarities, suggesting that the same underlying representations are being used in both cases. Given such results, it is not surprising that people sometimes confuse images for percepts and vice versa. Indeed, "seeing" images that are not really there is precisely the problem in some neurological and psychiatric disorders where the person is deemed to suffer from visual hallucinations.

Behavioural data have not convinced all psychologists that there is a commonality between imagery and perception. Many maintain that imagery utilises more abstract, non-visual, language-like representations. Pylyshyn (1981) has suggested that the reason behavioural data appear to support the "reality" of visual imagery might result from subjects simulating the use of visual representations using non-visual representations. Anderson (1978) concluded that no behavioural data could ever distinguish alternative, non-visual, theories of imagery from the visual perceptual theories. However, more decisive evidence on the relationship between imagery and perception comes from neuropsychological measures in normal and brain damaged subjects. These experiments provide direct evidence on the internal processing stages intervening between stimulus and response in imagery experiments. Advances in techniques such as functional magnetic resonance imaging (fMRI) have also allowed fresh data on visual imagery to be gathered.

The new theoretical frameworks for imagery and perception raise the intriguing question of how we distinguish reality from imagination. In one theoretical account that has been postulated, and discussed later in this chapter, imagery and perception both share the same temporary storage system into which representations are "recognised". How then do we distinguish imagined and perceptual events?

This thesis will examine the close relationship between perception and imagery; this is achieved in two sections. First, neuroimaging studies on normals elucidate the neural structures that support perception, imagery and the perception of illusions, while section two reports on a neuropsychological investigation of a clinical group with visual hallucinations.

1.1.2 The history of visual imagery

Beginning with Wilhelm Wundt, the subject of imagery occupies an important place in the history of psychology. Wundt's goal was to document the basic sensations which comprised all experience and to determine the ways in which these elements combined. In an attempt to solve this problem, Wundt used the methodology of introspection as a way to study the structure of images.

Wundt felt that a strong relationship between perceptual representation and imagery existed and that, in fact, all thought processes were accompanied by imagery. However, by 1913 Oswald Kulpe and other researchers conducted several experiments, which led to the discovery that some thoughts were, in fact imageless. In the first experiment of this kind, subjects engaged in a weight discrimination task after lifting two weights. When asked how a judgement had been made, subjects replied that

instead of a judgement preceded by a series of syllogistic thought steps, the judgement appeared to come to mind all at once. Based on these initial reports, some researchers concluded that the Wundt's approach of introspection was not a fruitful way to study imagery.

In 1913, John Watson claimed that imagery was a process of "subvocal thinking". Watson and the behaviourists who followed him tried to eliminate all discussion of the mind or mental events (Watson, 1913). They attempted to explain behaviour by declaring that particular stimuli were associated with particular objectively specifiable responses. References to subjective phenomenon, such as thinking and imagery, were prohibited. From 1915 to the early 1960's imagery and the notion of mental representation in general took a back seat to the study of external behaviour.

During the later half of the century, the study of the structures and processes of thought fell back into favour as a valid topic of research. This return to favour was influenced, in part, by the apparent limitations of behaviourism in explaining certain aspects of behaviour. Human behaviour depends on what has been previously attended to, encoded and comprehended. Therefore, a response must be understood in terms of what is stored and known by the person eliciting the behaviour.

A variety of procedures have been used to determine perceptual-imaginal similarities. Such interest grew out of the development of componential approach to cognitive processes (Posner, 1978). To deduce the information processing operation involved in different tasks, performance data was collected on how long it took people to perform tasks under different conditions. This was the first step in the examination of mental

events and provided a productive scientific technique for the study of imagery. One consequence of this approach of collecting large amounts of behavioural data from normal subjects, and computer modelling, was a componential model of visual imagery (Kosslyn & Shwartz, 1977; Kosslyn, 1980). The development of a detailed model provided a theoretical platform for mental imagery that allowed testing of specific hypotheses about different components of imagery.

1.1.3 Kosslyn's model of visual imagery

Researches like Finke (1989), Kosslyn (1980,1983) and Farah (1984) have proposed that mental imagery comprises of several cognitive subprocesses that, in the brain, might otherwise be dedicated to visual perception. Each of these researchers explains imagery processes in different terms, and each provided a theory to account for the phenomenon.

Perhaps the most detailed is a computational account of visual imagery proposed by Kosslyn (1980). He begins by defining the medium in which images appear in a two-dimensional Euclidean space, referring to it as the "visual buffer". The visual buffer is a multiscaled, spatially organised structure that corresponds to a set of retinotopically mapped areas in the occipital lobe. Thus, the activation of the array of cells in the visual buffer (which is a consequence of some object being in the visual field) results in a pattern of activation that is isomorphic to the shape of the object provoking this activation. The stimulus object need not be visually perceived, but can be generated from information about the object that is stored in long-term memory. Thus, spatial and pictorial information that we consciously experience as an image, consists of a pattern of activation in the visual buffer. Kosslyn's visual buffer is considered to have certain

invariant properties, such as visual angle and grain, which are independent of the image that is "displayed " in it. Moreover, Kosslyn suggests that there are size constraints within the visual buffer. The grain of the medium determines what can and cannot be represented clearly. It also means that when an image is reduced in size, then parts of it may disappear. The spatial medium is also like a physical space in that it has a limited extent and is bounded, with an area of highest resolution at the centre. If images move too far in one direction they will overflow the medium.

The visual buffer is considered to be a short term memory structure in which representations of objects begin to fade virtually as soon as they are created, and as such the image needs to be continually refreshed by resampling the information stored in long term memory. Long term memory, according to Kosslyn's theory, contains two types of data structures: images file and propositional files. Image files contain stored information about how images are represented in the spatial medium and have an analogical format. Propositional files contain information about parts of the objects and how they relate to one another. These files are in propositional format. It is the information in these files which "maintain" the image in the visual buffer.

The visual buffer contains much more information than can be processed at the same time, so an "attention window" selects a region within the visual buffer for detailed processing and seems to operate in the same way for perception and imagery. Once an image has been encoded in the visual buffer, and attended to by the attention window, the image may require further processing. This Kosslyn suggested is accomplished by a series of processing modules. There is a distinction between modules that use the image as input, from those using long-term memory representations as the input. The

former includes such modules as FIND (i.e., examines and defines the image), RESOLUTION (i.e., improves the clarity of the image), REGENERATE (i.e., prevents the fading of images when maintaining them over along period of time). Another group of modules can reorganise depicted patterns, including ZOOM, PAN (i.e., the opposite of zoom), TRANSLATE (i.e., to move), ROTATE, SCAN and PARSE (i.e., refreshes selected segments of objects, thus creating new images). The main processing module that is active in the retrieval of images from long term memory is called IMAGE, this then breaks down into three subprocesses: PICTURE (i.e., recreating the appearance of objects from co-ordinate points stored in memory), PUT (i.e., co-ordinate separate encoding and fuses them into a single image) which is closely connected with FIND (i.e., used to "see" where a currently encoded image belongs within a PICTURE). According to Kosslyn's theory, input from the eyes automatically fills the visual buffer. An additional processing module named LOAD serves the purpose of maintaining the perceptual input from the eyes while simultaneously suppressing subsequent visual input. This module, therefore, is a counterpart of the PICTURE module with the difference being that a former receives input from the eyes, and the later from long-term memory. Using these modules, encoded images can be mentally transformed and then examined.

Kosslyn's work had two important strengths: first, by specifying in computational terms the different subprocesses that are involved in imagery, he silenced criticisms of vagueness that had been levelled at research into imagery and second, he supported his claims with empirical evidence.

According to this model, imagery shares several of the representations and processes of visual perception. When an object is perceived its appearance is encoded from the retinal images into the visual buffer. Here it may then be matched with long term memory, and hence recognised or it can be inspected or transformed. Kosslyn (1994a) later developed his theory of the relationship between visual perception and visual imagery. According to this model the difference between a percept and imagination lies in the route by which activity in the buffer is generated. Imagery is merely the reactivation of a spatial sequence of code that would have been created by perception. On this account, imagery and perception share their end-point (the visual buffer) but not their routes. Kosslyn's most recent version of his theory is more complex and integrates visual attention, memory and object recognition. However, the central notion that perception and imagery both involve activation within a shared buffer remains.

1.1.4 Reality testing and reality monitoring

If as Kosslyn argues, both visual perception and visual imagery involve attentional allocation to relevant attributes at spatial locations in the visual buffer, how can we distinguish reality from imagination? The same question can be asked about an auditory stimulus, if the articulatory loop is activated in both real and imagined voices, how can we distinguish between a real and imagined voice. Because real perceptual events are located "out there" in the world and imagined events are located "inside" our heads, it has sometimes been suggested that the defining criterion for a hallucination is that an inner event is wrongly projected into external reality. The problem of accounting for how most people distinguish perceived from imagined events has, until recently, been strangely neglected in the study of imagery. Understanding how the perceptual and imagery system may fail in hallucinators can

give important clues about its normal functioning, as well as giving new insights into the metacognitive processes.

1.1.5 Hallucinations

According to theory developed here the source from which the information is obtained is the difference between imagery and perception. The source of the perception is external sensation, and that of imagination lies with self-generation. Therefore, if the misattributed event is inner speech or verbal thought, then hallucinations will be auditory. If however, it is visual imagery that is misattributed then the hallucinations will be visual. Indeed, this is the basis of Frith's cognitive account of the nature of hallucinations in schizophrenic patients. According to Frith (1992), schizophrenic hallucinators who report hearing voices may have a failure in "self-monitoring" i.e. they fail to distinguish information in articulatory loop derived from self rather than outside events.

Mintz and Alpert (1972) suggested that hallucinations in schizophrenia might arise as a result of failed reality monitoring combined with vivid imagery. They found that hallucinators were more responsive to Barber and Calverley's (1964) "White Christmas" test. The subjects were asked to close their eyes and listen to a recording of "White Christmas," which was not in fact played. Heilburn hypothesised that hallucinators misattribute self-generated experiences to an external agent (Heilburn, 1980), and that they should be relatively poor at recognising their own thoughts. The skill of judging the source of a perceived event or, reality discrimination, would therefore seem to fall into the general domain of knowledge about cognition, or

metacognition (Flavell, 1979). A failure of this skill might cause a person to misattribute internal events to an external source and thus bring about hallucinations.

1.1.6 Studying visual imagery

So, is visual imagery really visual, and does it involve the same neural structures as perceptions? The subjective similarity of seeing and imagining suggests a common internal representation might underlie these two experiences. In support of this hypothesis, many experimental paradigms have gathered evidence that imagery and perception have similar behavioural consequences (as described in Section 1.3). However, for reasons to be discussed later in this thesis, not all cognitive psychologists find these behavioural demonstrations persuasive. It is therefore, of interest to turn to neuropsychological and neurophysiological evidence on these issues.

In recent years brain imaging techniques have provided a unique opportunity to identify, within the human brain, activity patterns related to particular aspects of imagery. Emerging from this work is the view that visual imagery involves the activation of visual areas in the prestriate occipital cortex, parietal and temporal cortex, and these represent the same kind of information in imagery as they do in perception. Moreover, different components of imagery processing (Kosslyn, 1980) appear to be differentially lateralised. The generation of visual images from memory depending primarily on structures in the posterior left hemisphere (D'Esposito et al. 1997), and the rotation of mental images depending primarily upon structures in the posterior right hemisphere (Alivisatos et al., 1997). Finally, in addition, neuroimaging techniques have provided new insights into the functional specialisation within the visual system

for imagery and perception. This thesis aims to further explore this functional relationship.

1.2 The Visual System

1.2.1 Functional neuroanatomy of the visual system

Around thirty years ago, the notion of two visual systems or pathways emerged (Schneider, 1969). These pathways were the "what and the "where" pathways. The major "what" pathway runs from the retina to the lateral geniculate nucleus, and then travels to the visual cortex reception area in the occipital lobe. The "where" pathway travels to the occipital lobe via the colliculus and pulvinar to many areas of the cortex including those responsible for turning the gaze toward an object (Andersen, 1989). Miskin et al., (1983) expanded further on this theory and added new divisions within these pathways. Work on primates involved the identification of multiple visual areas in the prestriate cortex and exploration of their organisation. A summary of the major cortical areas and connections is shown in figure 1.1. Since then, in the nonhuman primate at least 32 visual areas beyond the primary visual cortex (V1) have been identified.

What we can learn about the human visual system by studying non-human primates may be limited. The introduction of sensitive and relatively non-invasive neuroimaging techniques have now made it possible to map cognitive functions in humans. However, these techniques are still relatively new and knowledge of information processing carried out in homologous regions of the primate brain assists with the interpretation of the functional studies. Moreover, whilst human brain imaging techniques may predict the involvement of particular brain regions, they are unable to yet determine either the

nature of the inputs or main pathways afferent and efferent to these regions. Such data may be obtained by electrophysiological and pathway-tracing techniques in non-human primates.

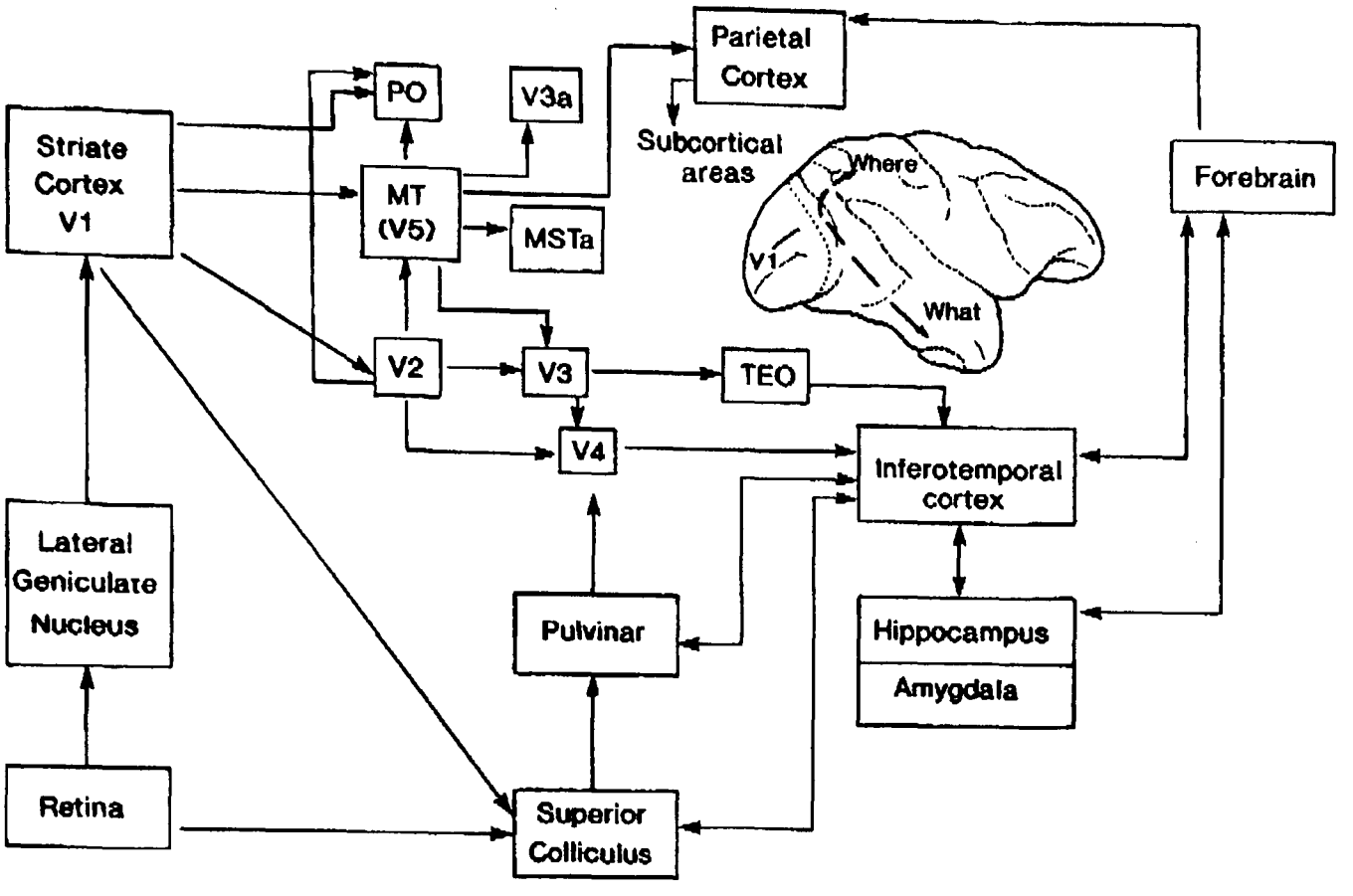


Figure 1.1
The major cortical areas concerned with vision and the major connections Between them (from Davidoff, 1991)

1.2.2 The primate visual cortex

The major output from the retina runs via the lateral geniculate nucleus (LGN) to the striate cortex (area V1) in the posterior occipital lobe, and from here to the many extrastriate visual cortical areas. As mentioned earlier 32 distinct visual cortical areas have been identified in the macaque on the basis of anatomical, physiological and behavioural information (Felleman & Van Essen, 1991; Van Essen, 1985). This complex organisation supports a combination of both hierarchical and parallel processing in the visual cortex.

Two major processing streams originate within the retina and remain separate throughout the LGN before reaching the primary visual cortex V1. These systems are the parvocellular (P) and magnocellular (M) systems, and correspond to the form/colour and dynamic form/motion pathways, respectively. In V1 and V2, these streams are reorganised into a tripartite arrangement to form the parvocellular-blob system (PB) which codes for colour, the parvocellular system (PI) which codes for form, and the magnocellular system which codes for motion. (Livingstone & Hubel, 1988; Zeki & Shipp, 1988).

The motion sensitive streams projects through a series of cortical areas including V3 and V5 before terminating in the parietal cortex. The form sensitive stream (PI) projects from the striate cortex (V1/V2) to V4 and from there into the inferotemporal cortex. However, these processing streams are not isolated from each other, either anatomically or functionally (see Zeki, 1993a).

1.2.3 Motion module (V5)

The evidence for an area specialised for the processing of visual motion, area V5 (also known as MT), was first provided by lesion data (Zihl et al., 1983) and later by functional imaging studies (Zeki et al., 1991a; Watson et al., 1993; Tootell et al., 1995). Cells within this area are highly specialised for moving stimuli. Neurons can detect motion in all directions of the frontal-parallel plane as well as simple motion towards or away from the organism (Tootell et al., 1995). As defined by the technique of positron emission tomography (Zeki et al., 1991), area V5 occupies the temporo-parieto-occipital pit, at the boundary of Brodmann areas (BA) 19 and 37, a cortical region compromised in the patient of Zihl et al., (1983). In the macaque monkey, area

V5 is surrounded by satellite areas (Desimone and Ungerleider, 1986). These areas are involved with the processing of motion related information but in ways which differ from the role of V5. One such area is the medial superior temporal sulcus (MST). Neurons in this area respond optimally to expanding, contracting or rotating patterns. The location of the human equivalent of this area, V5A, has recently been identified in the human visual system using functional magnetic resonance imaging (fMRI) (Haug et al., 1998) however, as yet the relationship of V5A with other areas in V5 is poorly understood.

1.2.4 Colour module (V4)

In the visual system, colour is represented as a separate module from other properties of a visual stimulus, this modular input theory requires that brain damage could completely remove colour vision yet leave all other visual functions intact. Studies in the macaque have shown colour-sensitive neurons in an area called V4, located in the banks of the lunate sulcus in the lateral occipital lobes (Zeki, 1973; Zeki,1977). Lesions to this particular area of the primate brain lead to impaired colour vision (Wild et al., 1985), while removal of V4 brings about disturbances of hue discrimination (Heywood et al., 1992). Human area V4 has been localised to the lingual and fusiform gyri in ventromedial occipitotemporal cortex (Zeki, 1990), or more specifically to the fusiform gyrus (McKeefry & Zeki, 1996). Lueck et al., (1989), carried out the first imaging study utilising positron emission tomography (PET) to localised the colour centre. Subjects were shown a colour Mondrian display in the active condition, and the resultant regional cerebral blood flow (rCBF) was compared to that when viewing a equiluminous display containing shades of grey. The viewing of the coloured stimuli resulted in activity in both lingual and fusiform gyri, the activity being greater in the

left hemisphere. Zeki et al., (1991b) went on to expand upon these results, showing the maximum rCBF was seen in the fusiform gyri. Acquired disturbances of colour perception should therefore be an indication of occipital lobe involvement. A recent study used fMRI to compare the blood oxygenation in the brains of 12 human subjects while viewing a colour Mondrian with its achromatic version in 12 human subjects (McKeefry and Zeki, 1997). Although they found that the position of V4, defined functionally, in the individual can vary greatly, it was consistently found on the lateral aspect of the contralateral sulcus. No activation was seen in the lingual gyrus. Further investigations revealed the topographic map within V4. More specifically, human V4 located in the fusiform gyrus has a representation of both inferior and superior visual fields.

Clinical evidence now exists to support V4 as the colour centre. Cerebral achromatopsia is a disorder of colour perception as a consequence of lesions in the anterior inferior part of the occipital lobe (Meadows, 1974). Patients claim that they cannot see colours anymore and that "everything appears in various shades of grey" (Pallis, 1955; Meadows, 1974). Other disturbances of colour vision seem to be divided into two separate entities. Patients can show deficits identifying and sorting colours (colour agnosia), or show a defect in colour naming (colour anomia). Recent analysis of colour naming (De Vreese, 1991) supports the hypothesis that there are at least two types of deficit that can occur, namely a colour imagery disorder and another due to disconnection between the language areas and imagery areas.

1.3 History and Development of Neuroimaging Techniques

1.3.1 Background

The quest for understanding the neural processing in the normal human brain has in the past involved various behavioural and electrophysiological techniques. More recently, new techniques of functional brain imaging such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have allowed examination of how brain function supports mental activity. Both of these methods exploit the principle that neural activity in a particular area of the brain results in the corresponding change in local cerebral blood flow (CBF). Functional imaging has been applied to the study of the visual cortex in activation and correlation studies. In the former, normal subjects are given specific tasks and cortical regions "activated" or recruited by the performance of these tasks are monitored. In the latter, patients usually debilitated by some degree of brain damage are tested with the goal of identifying the cortical areas "inactivated" and presumably responsible for neuropsychological impairments. Two reviews (Haxby et al., 1991b; Perani et al., 1992) have detailed early efforts with PET to map the functional neuroanatomy of the cerebral cortex. In this section, the emphasis will be on fMRI methodology as it was the technique used for the studies in this thesis.

1.3.2 Functional magnetic resonance imaging (fMRI)

Functional magnetic resonance imaging (fMRI) is a technique developed within the last decade that uses an MRI scanner to detect changes in blood-oxygenation levels while subjects perform some kind of sensorimotor or cognitive task. Like standard MRI, it is non-invasive and highly repeatable as it depends on measuring the effects of radio frequency pulses on primary hydrogen nuclei in a static magnetic field. Currently

it can achieve a spatial resolution of less than a millimetre and a temporal resolution measured in milliseconds, although with standard systems performing whole brain imaging, spatial resolutions of a few millimetres and temporal resolutions of a few seconds are more common. The effect on which most fMRI depends is called blood-oxygenation-level-dependent (BOLD) contrast (Ogawa et al., 1990), which is achieved by choosing imaging parameters that are sensitive to the relative concentrations of oxy- and deoxyhemoglobin in the blood. FMRI gives the opportunity for researchers to view physiological changes within a human subject's brain while that person is performing some kind of sensorimotor or cognitive task. Virtually real-time, high-resolution measures of functional activation of the living human brain are thus, finally accessible to study by psychologists and neuroscientists.

1.3.3 Neural bases of fMRI

Echo-planar imaging (EPI) is the most popular method for creating functional images using MRI (Stehling et al., 1991). fMRI takes advantage of a difference in the magnetic properties of deoxyhemoglobin and oxyhemoglobin. Deoxyhemoglobin is paramagnetic, meaning it tends to increase the strength of a magnetic field. In contrast, oxyhemoglobin is diamagnetic, meaning that it tends to decrease the strength of the magnetic field. These different magnetic properties of haemoglobin's two oxygenation states produce localised magnetic field inhomogeneities that affect a parameter known as T2*. In particular, deoxyhemoglobin increases magnetic susceptibility and therefore decreases T2* by increasing spin dephasing of protons.

The cascade of events that determines the fMRI signal, and generates the signal for other functional neuroimaging techniques, is as follows: sensory, motor or cognitive

activity causes a localised increase in neural activity which produces an increased metabolic demand that is satisfied over the course of several seconds and regional blood flow gradually increases. The increased blood flow delivers a relative excess of oxyhemoglobin, thus decreasing the regions' magnetic susceptibility and producing an increase in the MR signal sensitive to T2*, termed blood-oxygenation-level-dependent (BOLD) contrast (Ogawa et al., 1990). Thus, the BOLD MR signal is taken as evidence of neural activity underlying the behavioural task or cognitive event of interest.

1.4 Rationale for Studies Reported

Visual Hallucinations (VHs), percepts in the absence of external stimuli, have been recognised as a symptom of brain dysfunction for over a century and may occur in association with known changes in brain structure or pathology. Indeed, VHs are the commonest hallucination in Alzheimer's disease (Lerner et al., 1994), have been reported in 40% of schizophrenics (Mueser et al., 1990) and are included in the diagnostic criteria for dementia with Lewy bodies (McKeith et al., 1992). The ability to interpret exogenous stimulation is an essential feature of the human visual system, if visual perception and visual imagery are to be interpreted separately. However, as common as VHs appear to be, the neural and cognitive mechanisms underlying them largely remain a mystery.

The studies reported here use fMRI to observe brain activation while normal subjects are performing comparable imagery and perception tasks. All the imaging studies utilise a technique called echo-planar imaging (EPI). This method is capable of detecting small changes in blood oxygenation levels (BOLD contrast, see Ogawa et al.,

1990) which represent functional activation of the brain in response to local increased metabolic demand from neurons. The goal of this work was to identify the functional roles played by different regions of the brain in "experiencing" visual "stimuli" of both external and internal sources. Comparison of these brain regions may reveal functional process underlying imagery and perception and possible sites of convergence between the two experiences. Depending on these it may shed light on the neurological processes underlying visual hallucinations.

Chapter 2: Methodological issues and Protocol

2.1 Regulations and Protocol

2.1.1 Ethics

Ethical issues that arise from studies detailed in this thesis include the consent of the subject and confidentially. In addition, with imaging studies the issue of detection of brain pathology has to be considered. Ethical permission for the studies in this thesis was obtained from the Bethlem and Maudsley Research Ethics Committee. Detailed information regarding the purpose and procedures of the study, and all the possible risks to the subjects were provided in advance.

2.1.2 Consent

All the subjects gave their informed and written consent for the studies following a verbal and written explanation of the procedure by both a radiographer and the investigator. Details of their medical history and past scans were recorded. Subjects were also given details of contraindications that would prevent them for being scanned. In accordance with MR unit procedures at the Maudsley hospital, all subjects were informed that their brain scans would be viewed by an experienced radiologist and in the event of a tumour or other anomaly being found, their General Practitioner would be notified.

2.1.3 Confidentiality

Confidentiality of information was assured for all volunteers described in this thesis. Subjects were informed that their data may be used in studies at a later data and that their identity would be protected in publications arising from the research. All data was stored under the conditions of the Data Protection Act.

2.2 Subjects

2.2.1 Recruitment

All the subjects that took part in these imaging studies were volunteers and recruited by direct approach from the investigator. Recruitment was among staff and students of Institute of Psychiatry and the University as well as the wider community.

All subjects were tested for handedness using Annett's (1967) hand preference questionnaire, which takes into account the fact that for many left-handed and ambidextrous persons, lateral preference is not easily dichotomised (Briggs & Nebes, 1975).

2.2.2 Exclusion Criteria

Due to the extremely high magnetic field involved in magnetic resonance scanning, subjects with cardiac pacemakers or metallic implants are excluded from investigation. Women who might be pregnant were also excluded from the investigations due to the current lack of information concerning the possible contraindications of high magnetic fields on the unborn. Subjects were also excluded if they had any history of psychiatric or neurological disease. As spectacles cannot be worn in the scanner, subjects with impaired vision which was not corrected to normal with contact lenses were also excluded.

2.2.3 Sample size

The sensitivity of fMRI does theoretically allow experiments to be carried out on individual subjects and enable the localisation of brain regions. However, the studies reported in this thesis used six or seven subjects. This was a trade off between the cost

of scanning and optimising the results. Groups of this size have previously been used successfully in visual cognitive tasks in fMRI (Cohen et al., 1996).

2.3 Procedures

2.3.1 Subjects

All the tasks performed in these studies were straightforward, however, all the subjects were given full instructions and training on each before entering the scanner. Subjects were asked to remove all metal objects from their person before being led into the scanning room and asked to lie flat on the scanner bed. Once subjects were lying down a radiographer assisted with positioning the subjects' head between cushioned supports and securing the headstrap. Headphones with ear sound protection were provided for subjects to protect them against the potentially damaging sound level of the scanner and to provide a means of hearing the radiographer and investigator throughout the experiment. The procedure consisted of initially taking the functional scans while doing the experiment and then once completed, a high-resolution inversion recovery scan was collected. This high-resolution scan was taken to facilitate the normalisation of data into standard stereotactic space of Talairach and Tournoux (1988).

2.3.2 Stimuli

Visual stimuli were either shown from video or a personal computer. Stimuli was projected onto a screen located at the base of the scanner bed via a Proxima 8300 LCD projector. Subjects were able to view the stimuli while lying down through a prismatic mirror located above their heads in the scanner.

2.3.3 Paradigm design

Using the technique of fMRI, the experimental design that was employed to localise brain functions was periodic stimulation. The paradigm consists of alternating epochs of an "ON" experimental condition and an "OFF" baseline condition, and assumes that cortical activation in the experimental phase will show the regions involved in the task under investigation.

This approach is referred to as "cognitive subtraction" (Donders, 1869). Statistical methods of data analysis are highly developed for such paradigms and as such it is this method that was used in this thesis. The weaknesses inherent in this approach become apparent when attempting to isolate the constituent components of a cognitive task. The functional difference between the "ON" and "OFF" phases is a subtraction of one "active" phase against another "active" phase with no resting condition. This cognitive subtraction method assumes "pure insertion". This asserts that one can add a new component into a task without affecting the implementation of a pre-existing strategy. However, the fallibility of this assumption has been acknowledged for some time (e.g. Sternberg, 1969) and has been demonstrated by the modulation of sensory processing by directed attention (Corbetta et al, 1991).

The way forward is now being reflected by the employment of factorial and parametric designs in fMRI studies. These approaches either examine the interaction between factors; specifically the effect of one factor on the responses to other factors, or as in parametric designs, treat cognitive components as dimensions as opposed to categories.

2.4 Data acquisition

2.4.1 The Hardware

The data reported in this thesis were acquired using a 1.5 Tesla GE Signa system (General Electric, Milwaukee, U.S.A.) retrofitted with Advanced NMR hardware (ANMR, Woburn, MA, U.S.A.). Radio frequency transmission and reception was achieved using a quadrature birdcage coil, which encompasses the whole head.

2.4.2 Quality control

As BOLD fMRI studies at 1.5 Tesla rely on very small increases in signal intensity during activation, these changes may be masked either by artefacts or temporal system drifts. In addition, echoplanar imaging (EPI) is particularly susceptible to Nyquist ghosts caused by misregistration of alternate lines in time acquired data (k-space). These ghosts manifest themselves as a low signal copy of the image shifted (or "wrapped around") by a distance equal to half the field of view. At the MRI Centre at the Maudsley Hospital, appropriate calibration is carried out on a daily or scan-by-scan basis to eliminate, or at least minimise, their effects. Temporal drifts in signal intensity can also occur due to gradient instabilities and changes in temperature of electronic circuitry. Phantom scans are also carried out on a daily basis to ensure temporal stability (Simmons et al., 1997).

2.4.3 Image acquisition

Extremely fast imaging methods are needed to "capture" brain activation in a cognitive task. The technique used for the studies reported in this thesis is echo planar imaging (EPI). This is an ultra-fast, MR imaging method which allows capture of a full single slice image after the application of only one radio frequency pulse in a total

acquisition time of less than 100 ms. However, there are disadvantages to this technique. The need for a wide receiver bandwidth leads to a reduction in signal-to-noise ratio, and the requirement to sample data for long acquisition times after each excitation can lead to increased image distortion, due to a higher sensitivity to magnetic field inhomogeneity. Nevertheless, the very rapid data acquisition still makes EPI the optimal choice for multi-slice functional neuroimaging experiments and the pitfalls may be minimised by implementing field mapping and subsequent distortion correction algorithms. The hardware requirements for such a method include very rapidly switching magnetic field gradients controlled by powerful current amplifiers, and wide receiver bandwidth technology to allow an extremely high signal-sampling rate.

For all EPI functional scans reported in this thesis, 100 T2*- weighted MR images depicting BOLD Contrast were acquired at an echo time TE=40ms, and repetition time TR=3000ms, in each of the contiguous planes parallel to the intercommissural plane. These comprised 14 x 7 mm thick slices with an 0.7mm interslice gap (except for the data collected in Chapter 4 which comprises 10 x 5.0 mm thick slices with an 0.5 mm interslice gap). Each 2-D image matrix comprised 128 x 64 voxels, each of which had a 16 bit integer value for signal intensity for each subject. A 43 slice, high resolution inversion recovery, gradient echo, echo planar series of the whole brain was also acquired parallel to the intercommissural (AC) plane with TE = 4Oms, TI = l8Oms, TR = l6 secs, in plane resolution of 1.5mm, slice thickness = 3mm (8 data averages) in the same session. These echo planar images allowed direct superimposition of voxels from the time series without correction for geometric

distortion which is necessary when functional maps are registered onto conventional MR images.

2.5 Data analysis

2.5.1 Signal to Noise Ratio

Signal-to-noise ratio (SRN) is one of the most important parameters in functional imaging studies. The factors that determine the SNR are the size of the volume elements (voxels) in the image, the amount of T2* signal generated by the pulse sequence, and the number of repetitions of either the pulse sequence or trials of the task. Increasing voxel dimensions proportionally increases SNR, however SNR improves only with the square root of the number of repetitions. The signal is a function of the number of excited protons and their degree of excitation. Both these parameters are determined by the field's strength B_o and the flip angle used in the pulse sequence. Noise in fMRI comes from three sources: thermal noise within the subject, thermal noise within the scanner electronics, and magnetic field inhomogeneities. The first two noise sources are fixed for a given subject and scanner, but the third is usually reduced by applying shimming gradients to try to make B_o as uniform as possible for each scanning session. Thus, adjustments to the scanner can minimise the noise, and the most direct way of increasing signal strength without comprising spatial resolution is to increase the number of trials collected.

2.5.2 Motion artifact as a source of variability

A second issue affecting the interpretation of data is the presence of motion artifact. A variety of methods have been developed to try to prevent motion artifact in fMRI data from head motion itself, and several post-processing algorithms have been developed

as well. One possibility for limiting subject head motion is to have them bite down on a dental mould affixed by a bar to the head coil, called a bite bar. The main problems with this method are that biting down on an object for a long period of time can produce fatigue in the jaw muscles and that it increases salivation and therefore causes the subject to swallow more frequently, which is an additional potential source of motion artifact. A second method for preventing motion artifact is to create a rigid head mould from a porous sheet of thermoplastic. This approach has the advantage of being relatively rapid to set up and makes reliable placement more practical for repeated studies on the same subject. Its main disadvantages are that it can become quite uncomfortable if the study requires much more than one hour to complete and that time must be allowed before the initial session to prepare the mask. Also, the masks have a tendency to shrink somewhat if they are made more than a day or so in advance of the study. The masks also give the illusion of holding the subject's head still, but the subject may nonetheless move his or her up to a centimetre or so without much effort. The third approach and the one used in the following studies, is to try and make the subjects as comfortable as possible using padding around the head and neck and strapping around the forehead to remind the subject to keep their head still. This method has the advantage of being relatively quick to set up and alter if necessary. In addition, for long imaging studies, the more comfortable the subject is, the less they tend to move.

2.5.3 Movement estimation and correction

Slight subject motion during functional MR image acquisition can cause changes in T2*-weighted signal intensity unrelated to changes in BOLD contrast. The following procedure was adopted to estimate and correct the effects of motion prior to any

further analysis of the images. Firstly, "base" images of the mean signal intensity over time were created by averaging the 100 match images acquired in each plane.

The sum of absolute differences in gray-scale values between the match images acquired at each time point and the base image volume was computed.

A multi-dimensional search by the Fletcher-Davidson-Powell algorithm (Press et al., 1992) was used to find the translations and rotations in three dimensions which minimised the total absolute difference between each match volume and the base volume. The match volumes were realigned relative to the base volume by tricubic spline interpolation. The T2*-weighted signal intensity time series at each voxel of the realigned images were regressed on the concomitant and lagged time series of estimated positional displacements at each voxel (Friston et al., 1996). The residual time series resulting from the last stage of this procedure are uncorrelated with estimated rigid body motion in 3D.

2.5.4 Generic Brain Activation Mapping

Statistical techniques for estimating the experimental effect on fMRI time series data are widely debated in this field. The inherent problem is that neuronal activation only induces small intensity changes. Even after a decision has been reached about the best method for estimating the experimental effect, the next question concerns whether or not the observed effect is significant and how best to decide on the significance level which provides the optimal balance between Type 1 and Type 2 errors (see reviews by Rabe-Hesketh et al., 1997; Lange, 1996).

The data reported in this thesis were analysed using the method developed by Bullmore et al, (1996) which has been extensively validated at the Institute of

Psychiatry and other centres, and compares favourably in sensitivity with all other published methods available at the time of this study. First, the power of periodic signal change at the (fundamental) ON-OFF frequency of stimulation was estimated by iterated least squares fitting an 8 parameter sinusoidal regression model (intercept, linear drift, and pairs of sine and cosine terms at the stimulus frequency and its first and second harmonics) to the motion-corrected time series at each voxel of all images. The fundamental power quotient (FPQ = fundamental power divided by its standard error) was estimated at each voxel and represented in a parametric map.

Since fMRI time series data is not normally distributed, and theoretical null distributions insufficiently accurate, non-parametric distribution free methods such as randomisation have proved most suitable for ascertaining critical values for testing the significance of activated voxel clusters (Poline and Mazoyer, 1993; Bullmore et al, 1996). To this end, each observed fMRI time series is randomly permuted 10 times, and FPQ re-estimated after each permutation. This results in 10 parametric maps (for each subject at each plane) of FPQ estimated under the null hypothesis (Bullmore et al., 1996). All parametric maps of FPQ are then registered in the standard space of Talairach &Tournoux (1988). This is achieved in two stages, using realignment algorithms similar to those previously used for movement correction. First, the set of FPQ maps observed in each subject is registered with that subject's high resolution EPI dataset; then registered and re-scaled relative to a Talairach template image. Identical transformations are applied to the randomised FPQ maps obtained for each subject. After spatial normalisation, the observed and randomised FPQ maps from each subject are identically smoothed with a Gaussian filter (full width half maximum = 7 mm) to accommodate variability in gyral anatomy and error of voxel

displacement during normalisation. Generic activation is then robustly decided by computing the median value of FPQ at each voxel of the observed parametric maps, and comparing it to a null distribution of median FPQ values computed from the randomised parametric maps. If the observed median FPQ exceeds the critical value of randomised median FPQ (which for the data in this thesis was typically a test of size $\alpha = 2.5 \times 10^{-4}$) then that voxel is considered generically activated with probability of false positive activation = α. At this level of significance, 10 voxels are expected to be "activated" by chance over the whole median image. Generically activated voxels are coloured and superimposed on the grey scale Talairach template, to create generic brain activation maps (GBAMs) (Brammer et al., 1997)

2.5.5 Phase analysis

The sine and cosine coefficients at the frequency of alternation of the ON and OFF conditions (gamma and delta) can be used to derive phase information for the response. The phase is computed as tan-1 (delta/gamma). This phase information can be shown for each voxel. A simple phase map can be constructed by simply examining the sign of gamma. If the experiment starts in the OFF condition and gamma is negative, the response is "in phase" with the ON condition. Whereas if gamma is positive, the response is out of phase" with the ON condition.

2.6 Display of Analysed Images

Data obtained in this thesis (Chapters 3-5) were rendered onto a high resolution spoiled GRASS (SPGR) template, previously mapped into Talairach space. The template of 25 x 5.5mm thick slices represented as a series of oblique axial slices in the AC-PC plane. This allows identification of the standard stereotactic co-ordinates

in each regional focus of generic activation. Datasets obtained were transformed into Talairach space and displayed on the template to identify Brodmann co-ordinates

2.7 Why fMRI?

Both PET and fMRI have their unique advantages and a number of factors must be taken into account when opting for a method by which to investigate a particular aspect of brain function. The most obvious advantage of fMRI is that it does not necessitate the injection of potentially harmful radioactive substances. FMRI additionally lends itself to single subject analysis or smaller sample sizes whilst retaining information on individual variability.

In spite of its many benefits, fMRI does have some limitations. One substantial difference between PET and fMRI is that the latter does not currently provide quantitative measures of physiological parameters. PET can measure absolute blood flow, but BOLD contrast detects only signal change between control and activation conditions, using the signal intensity of T2* weighted images. Furthermore, whilst there is a measure of consensus concerning the optimal statistical analysis of PET data and the subsequent displaying of images (Friston et al, 1991), the same platform has yet to be reached for fMRI data. However, in view of the rapid developments in fMRI methodology, the application of generic analytic techniques may not be appropriate. A more practical issue concerns the extremely loud noise produced by the rapid switching of currents through the gradient coils during an fMRI scan. Although theoretically any stimulation which is consistent during all experimental conditions should be subtracted out in the subsequent analysis, in practice, it is not yet known whether the noise interferes differentially in the perception of stimuli in one condition

more than another. By comparison with PET, fMRI is more sensitive to subject motion, which can cause substantial distortion to the image. However, normal motion artefacts can be considerably reduced by subsequent analytic strategies

Whilst fMRI offers better temporal resolution than PET, it is unable to compete with the millisecond monitoring of neural activity offered by event-related potentials (ERP's) or magnetoencephalography (MEG). However, the advantages of this temporal precision are substantially offset by the very poor localisation potential of these techniques, particularly in subcortical structures. Future research will undoubtedly witness a merger between the temporal resolution offered by the latter methods and the spatial superiority of fMRI. However, at present, the availability of fMRI, the marked superiority in spatial resolution offered by fMRI, together with fast acquisition times which facilitate studies, makes it the obvious choice for the studies presented here.

2.8 Application of fMRI to Visual Research

The mapping of the visual system utilising MRI technology has allowed insight into its structural and functional architectures. Functional MRI has been used to determine the borders of human visual areas V1, V2, V3 and V4 (Sereno *et al*, 1995), activation of area V5 by visual perception of motion (Howard *et al.*, 1996) and functional specialisation within the motion related visual cortex (Howard *et al.*, 1996). Area V5, posterior to the junction of the ascending limb of the inferior temporal and lateral occipital sulci, is specialised for the perception of coherent motion (Zeki, 1991a; Watson *et al*, 1993; Tootell *et al*, 1995), optical flow (de Jong *et al* 1994; Howard *et*

al, 1996), biological motion (Howard *et al*, 1996), and illusory motion (Zeki *et al*, 1993b; Tootell, 1995).

As already noted, functional neuroimaging with normal volunteers and patients with acquired deficits in colour perception has enabled the human colour area (V4) to be localised to the lingual and fusiform gyri in ventromedial occipitotemporal cortex (Leuck et al., 1989; Zeki et al., 1991a) or more specifically, to the fusiform gyrus (McKeefry & Zeki, 1997). The studies reported here use fMRI to observe brain activation while subjects are performing high-level visual tasks. The goal of this work was to identify the functional roles played by different regions of the brain in visual imagery.

SECTION 2: NEUROIMAGING STUDIES IN NORMAL SUBJECTS

Chapter 3: Cortical activation during rotational and linear transformations

3.1 Introduction

3.1.1 Background

The topic of mental rotation has captured the interest of psychologists for the past few decades. In a typical mental rotation experiment, subjects are shown drawings of a standard and a test object. The test object is presented at an orientation that differs from the standard object's orientation and over trials the angular disparity between the two objects is varied. Upon viewing these objects, the subject must decide as quickly as possible whether they depict the same shape. In past experiments, object pairs have consisted of either three-dimensional, cube assemblies (Shepard & Metzler, 1971; Yuille & Steiger, 1982), drawings of familiar patterns such as letters and numbers (Cooper, 1975; Cooper & Podgorny, 1976) and polygons (Cooper, 1975; Cooper & Podgorny, 1976). Subjects in these experiments are able to identify two shapes as being identical or different, although performance levels have varied across studies. Even though standard and test objects differ in orientation, viewers are somehow able to "manipulate" one or both of these objects in such a way that a comparison between the two shapes can be made. It is the nature of this "manipulation" that has been the focus of the research.

3.1.2 Theories of mental rotation

A variety of theories that address the nature of the mental rotation process have been generated. The argument in divided into two camps: the propositional theorists (Anderson & Bower 1973; Clark & Chase, 1972; Pylyshyn, 1973, 1981; Reed 1974)

and the analog theorists (Farah, 1984; Kosslyn & Pomerantz, 1977; Kosslyn, 1980,1983; Pavio, 1971,1986; Shepard & Metzler, 1971). The propositionalists (or descriptionalists, as they are sometimes called) believe that all internal memory representations are in a propositional format. Instead of the representation depicting the physical referent, as in a picture, it describes it, as in a sentence. Therefore, images are represented symbolically as structural descriptions.

A structural description is a data structure that comprises of a set of propositions. Propositions are abstract symbol structures that express relations between concepts. Although propositions are not linguistic structures, they can often be approximated by simple sentences. In the case of propositional representation approximated using English words to describe an image of a ball on a box, the words "ball" and "box " are the arguments and their relationship to one another is specified by the word "on".

Propositional representations differ from quasi-pictorial image representations in many ways. First, they are largely unconscious. Second, they do not occur in a spatial medium as a real world perception would. In fact, propositional representations do not assume any medium, as their properties are not dependent on a supporting structure. Because a spatial medium is not required, there is no isomorphism between object and space. Third, they specify actions and relations which images do not necessary do. For example, as Wittgenstein (1953) noted, an image of a man standing on a hill might be interpreted as a man either walking up a hill or walking down the hill. In order to assign meaning to an image representation subsequent processes would be necessary. In contrast, in a propositional representation corresponding to a picture of man on the

hill, the specific activity assigned to the man would be inherent in the representation itself.

In contrast, the analog theorists believe that there is a quasi-pictorial imagery representation that is very much like its physical referent in the real world in that it is thought to occur in a mental spatial medium which is functionally equivalent with a co-ordinate space. It therefore shares properties with a physical medium, such as relative size, shape and colour. In fact, when the analog theorists speak of imagery, the image may be referred to as a "picture in the head" and "seen with the minds eye". Because the image may be thought of as akin to a mental photograph, a point to point correspondence between the parts of the image and the parts of the real world object is thought to exist. That is, the pattern of the spatial image is in essence a topographic mapping from the represented object. In this way, each section of the image corresponds to a section of its real world physical object as viewed from a particular point. Furthermore, the distances between sections of the image are consistent with those of the imaged object. Therefore a spatial map exists between parts of the real object and parts of the image that depicts that object.

In summary, the analog theory posits a pictorial representation and a transformation that is analogous to a physical transformation of a real object through real space. This theory is specific as to the nature of both representation and transformation. The propositional theory is most specific with regard to imagery representation, which is thought to be comprised of a structural description. However, the propositional theory of transformation is not explicit in that it does not clarify the nature of the transformation that operates upon the representation. Although the propositionalists

advocate that the transformation occurs when there are propositional changes, the relationship between specific propositional substitutions and degree of rotation has not been stated. Therefore, the propositional theory is more a theory of representation than transformation.

The preceding overview presented theories of imagery representation and transformation that are relevant to visual imagery and mental rotation experiments. In the following section, the research that has been generated from these theories will be reviewed.

3.2 Literature Review

3.2.1 Behavioural studies

Shepard and Metzler conducted the first experiment concerning reaction time as a function of angular disparity during a mental rotation task (Shepard & Metzler, 1971). In this classic study, drawings of three-dimensional, cube assemblies were presented to subjects. The task was to decide, as quickly as possible, if a comparison object was identical to a standard object. The comparison object was not depicted in the same orientation as the standard. In order to judge if the comparison object was identical to the standard, Shepard and Metzler predicted that a mental rotation of the comparison either in depth or in the picture plane would ensue until the orientation matched that of the standard. In an attempt to force the subjects to carry out a mental rotation in contrast to responding on the basis of some simple distinctive features, the "different" comparison objects consisted of mirror-images of the standard. In this way, subjects could not simply rely on single distinctive features of the forms in making their judgements.

The results revealed an average performance score of 98.8% correct. Therefore, even though subjects were responding as quickly as possible, they were still able to achieve high performance scores. The results also showed that reaction time was an increasing linear function of the angular disparity between the two patterns and that to rotate in depth was virtually the same as time to rotate in the picture plane. When the slope of these two functions was examined, an average rotation rate of 60 degrees per second was derived. Shepard and Metzler concluded that subjects were imagining one of the forms rotating at a constant rate into alignment with the other form because of the proportional increase in response time. Furthermore, since the speeds of imagined rotation for the angular disparity in the picture plane and in depth were identical, they concluded that it was not the two-dimensional shape of the picture that was rotated but the three-dimensional shape of the object. Therefore, it appeared that subjects were performing a mental rotation in a three-dimensional space and that this rotation was an analog of the holistic rotation of an object. Subjective accounts were consistent with the objective evidence. Subjects reported that they imagined one of the two objects rotated into the same orientation as the other and checked to see that the two objects were congruent.

The previous study used cube-like objects as stimuli. In contrast, Cooper and Shepard (1973) conducted studies in which familiar patterns that had standard upright orientations were used. Cooper and Shepard reasoned that if subjects were indeed performing a mental transformation in the Shepard and Metzler (1971) task, then reaction time would fail to be a function of angular disparity if subjects knew, prior to viewing the standard stimulus, the identity and orientation of the comparison stimulus. In this way, subjects would be able to perform the necessary transformation prior to

test time and therefore time to respond would not increase with deviation of the comparison stimulus from the orientation of the standard.

In the first experiment (Cooper & Shepard ,1973), the test stimuli consisted of both letters and numbers presented in a circular aperture. Each of these was presented to the subject in one of six orientations. Orientations consisted of 60-degree steps around the circle starting from a standard upright position of zero degrees. The experimental task was to judge if the test character was in a normal or backward position. Prior to the presentation of this test figure, subjects received different information depending on the condition employed. The information conditions were as follows: 1) A line drawing of the character presented first in the circle and in its standard, upright orientation (identity-only condition). 2) An arrow presented in the circle, which indicated the orientation of the subsequent character (orientation-only condition). The arrow pointed to the location of the top portion of the character. 3) The outline of the character first appearing for 100 msec., in the actual orientation that the test figure would later appear in (combined-identity/orientation condition). 4) The identity of the character appearing, terminating, and then replaced with orientation information (separate-identity/orientation condition). This last condition was critical in that the duration of the orientation cue varied. It persisted for 100, 400, 700 or 1000 msec., after which it was immediately replaced by the actual test stimulus. 5) The test stimulus was not preceded by any information (no-advance-information condition). Cooper and Shepard hypothesised that if subjects were indeed performing an analog mental transformation, then the no-advance-information, orientation-only, and identity-only conditions should produce reaction times that were a function of test stimulus orientation, but that both the combined-identity/orientation and the separate-

identity/orientation condition with the long orientation cue persistence (1000 msec.) should not vary in this case. For the latter conditions, subjects would have time to perform a mental transformation prior to the onset of the test stimulus. For trials in which the orientation cue persistence was brief, subjects would not have sufficient time in which to perform this transformation.

When the data were analysed, the above hypotheses were confirmed. That is, for the no advance, identity-only, and orientation-only conditions, reaction time increased markedly as the angular disparity of that stimulus departed from its standard upright orientation. Furthermore, the advance information presented separately, for the 1000 msec. duration, produced a function as flat as the one found for the combined-identity/orientation condition. These findings supported the claim that subjects were mentally rotating a mental image of the anticipated stimulus prior to its presentation in the test phase. In a later study (Cooper and Shepard, 1975) a similar finding was obtained when subjects attempted to discriminate between rotated drawings of right and left hands. Subjects were not aided when orientation cues were provided without accompanying identity cues. Cooper and Shepard concluded that subjects used this rotated internal representation as a template against which they compared the subsequent test stimulus. However, to claim that there is an isomorphism between the mental and physical processes of rotation, the starting point, end point, and all intermediate points along the rotation trajectory should correspond in both mental and physical rotations. If this is the case, then it implies that a subject should respond fastest to an object presented in the orientation the subject has obtained at that particular moment. Cooper and Shepard (1973) conducted a second experiment in order to test this hypothesis.

In their second experiment, Cooper and Shepard (1973) instructed subjects to image either a letter or number rotating 60 degrees clockwise in synchrony with an auditory command. At a random point, a probe character was presented in a normal or backward version. On half of the trials this probe was presented in the orientation that the subjects should have been imaging at that particular time, and for the other half of trials it was not. The subjects' task was to decide, as quickly as possible, if the probe was presented in its normal or in its reversed version.

When the data from this second experiment were analysed, relatively flat functions were found for the trials in which the visual probe appeared in the orientation corresponding to the current auditory command. These results were similar to those of the previous experiment in which subjects had a 100 msec. advance time to rotate their mental image. In contrast to these results, when the probe stimulus differed from the expected orientation, mean reaction time was a function of angular departure. That is, reaction time increased as the orientation of the test stimulus increasingly diverged from that of the image. Pylyshyn (1981) argued that perhaps subjects do not rotate the comparison figure in a smooth continuous manner, but instead, because they have learned through testing which orientations will be probed, skip from one orientation step to another in the rotation sequence without imagining that the figure passes through intermediate orientations. Cooper (1976) however, conducted a study in which she showed that mental rotations do pass through these intermediate orientations even when subjects do not know that they will be tested at those orientations.

To explain the findings of the previous studies, Shepard proposed the principle of the 'second-order' isomorphism of internal representations which states that relations among internal representations of objects corresponded to relations among the objects themselves. Therefore, an imagined transformation would pass through all of the intermediate steps that its physical referent would pass through (Cooper and Shepard, 1973; Cooper, 1976; Shepard and Chipman, 1970; Shepard and Metzler, 1971).

Despite the impressive results that many of the mental rotation studies have yielded, the issues of task-induced demand characteristics and experimenter bias must be explored. Fortunately, mental rotation tasks are not as subject to task-induced demand characteristics as are other tasks such as scanning because more emphasis is placed on a correct and rapid response. As for experimenter bias effects, again mental rotation tasks are not as open to this criticism because the task is straightforward and there is little contact with the experimenter. Intons-Peterson (1983) has claimed that the intercept to the reaction time function in a mental rotation task can be influenced by the expectations of the experimenter but it has also been found that the motivation of the subject and the difficulty of the task can also affect the intercept (Cooper and Podgorny, 1976; Shepard and Cooper, 1982). Furthermore, it is quite doubtful whether the finding that reaction time is a function of angular disparity could be due to experimenter bias as this finding is very robust and has been found by both types of theorist. Tacit knowledge for how real transformations occur across physical distances could also influence the imagined transformations of objects (Pylyshyn, 1981). That is, for cognitively penetrable tasks, such as mental rotation, subjects could manipulate the outcome due to their beliefs about the nature of the task. If subjects knew that reaction time should increase with angular distance then this belief might have

influenced the nature of the responses. Subjects would attempt to temporally match their propositional transformations to the time interval they believe would actually occur in the real world. However, Cooper and Shepard (1973) found a difference between real and imagined rotations which could not have been predicted on the basis of tacit knowledge. Specifically, when subjects rotated alphanumeric characters, reaction times flattened out slightly when the angular departures were close to standard orientations. This probably occurred because once the comparison object was rotated almost to the required orientation, the rest of the transformation was unnecessary (Hoch and Tromly, 1978).

In summary, the results of these experiments indicate that imagery and perception have many similarities, in terms of the behavioural responses of normal subjects, suggesting that the same underlying representations are being used in the two cases. However, even if one finds analysis of behavioural data plausible as evidence for shared representations in imagery and perception, it would desirable to obtain more decisive evidence. Neuropsychological evidence may to be more decisive, as it provides direct evidence on the internal processing stage between the stimulus and response. There have been a number of neuropsychological experiments carried out in both brain-damaged and normal subjects that give fresh evidence on the issue of visual imagery. Recent technological and methodological advances have also helped to elucidate the nature of the functional equivalence at neuroanatomical level. Two types of evidence on the relationship between imagery and perception are available. The first concerns processing deficits of perceptual and imaginal stimuli in brain-damaged patients. The second involves non-invasive methods for measuring electrophysiological activity or regional cerebral blood flow.

Neuropsychological studies

The early evidence for the visual cortex being involved in internal imagery came from neurological reports of cortically blind patients (Symonds & Mackenzie, 1957). Many of these patients with cortical blindness, characterised by the loss of vision due to destruction of the occipital cortex appeared unable to use mental imagery, despite retaining other cognitive abilities. Although these subjects with impaired visual perception of objects have parallel deficits in their visual imagery abilities, there have been cases of impaired imagery despite normal visual perception (Riddoch, 1990: Goldenberg, 1992) and cases of preserved imagery in visual agnosia (Behrmann *et al.*, 1992: Jankowiak *et al.*, 1992: Servos *et al*, 1995: Dijkerman & Milner 1997). Thus, suggesting that some of the visual mechanisms needed for visual perception are not needed for visual imagery. As mentioned the process of mental imagery or "seeing with the mind's eye" has been separated into a variety of sub-components, consisting of generation, maintenance, inspection and transformation (Kosslyn, 1994). These different sub-components of visual imagery may have a separate anatomical localisation and as such have been investigated in isolation.

It is generally accepted that many forms of visuospatial processing are mediated by the right cerebral hemisphere (RH) (De Renzi and Faglioni, 1967; De Renzi et al., 1977). Researches are, however much less specific in addressing the question of which hemisphere mediates mental imagery and the mental rotation process per se. The latter is often assumed to be right hemisphere function since it may be often construed as within the general domain of visuospatial capacities. A number of studies, however, implicate a prominent contribution by the left cerebral hemisphere (LH) for aspects of spatial processing such as 3D maze learning (De Renzi et al.,

1977), determination of line orientation (Mehta et al., 1987), point localisation in space (Ratcliff and Davis-Jones, 1972), and various forms of mental rotation (De Renzi and Faglioni, 1967; Mehta et al., 1987; Mehta and Newcombe, 1991).

When reviewing visual half-field studies of mental rotation, one is confronted by a confusing array of results ranging from no hemispheric advantage, to either a LH or RH superiority, depending upon the nature of the stimuli to be rotated (e.g. letters versus non-verbal forms), and other subtle task demands placed on the participant (e.g. concurrent memory loads (Corballis and Sidey, 1993) or 2D versus 3D mental rotation).

De Renzi and Faglioni (1967) tested unilateral right and left hemisphere-damaged patients with and without visual field defects. Nine line drawing of an abstract nature were presented to the patients along with a single drawing the same as the other nine except for a 180 degree rotation. The subjects' task was to identify to identical drawing. Both left and right hemisphere damaged patients were impaired relative to controls.

Unilateral right and left hemisphere damaged patients were tested in a study by Butters and Barton (1970). Fifty patients with cerebral damage were tested on 3 tasks requiring the performance of reversible operations in space. The 12 patients with severe parietal signs showed impairment on 2 of the tasks, regardless of the hemispheric side of damage, while the 4 patients with mild parietal signs did not reveal deficits on any test.

Butters et al (1970) followed up these finding with a study of 16 patients with right hemisphere cerebral damage, 12 with severe and 4 with mild parietal signs, were administered 2 intra- and 3 cross-modal associative tasks as well as 3 tests requiring mental imagery. The 12 patients with severe parietal signs were impaired on tactile-tactile and auditory-visual matching and on all 3 spatial tasks, while the 4 patients with mild parietal signs did not reveal deficits on any test. Further testing indicated that the right parietals' impairments on the auditory-visual task were associated with an inability to decode the auditory patterned stimulus rather than to a failure in cross-modal associations. When the performance of the right hemisphere patients was compared with the data from left hemisphere patients, it appeared that the left parietal region might be dominant for cross-modal associations, but that both the left and right are important for mental rotations.

Authors sometimes report conflicting results within the same study. An example of such is Corballis and Sergent (1989). In this study, neurologically normal male and female college age participants and one commisurotomized patient were used. The commisurotomized patient underwent complete forebrain commisurotomy for intractable epilepsy at the age of 13. At the time of testing he was 35 years old. Rotated letters (F, P and R) were flashed to the participant's left or right visual hemifield. The flashed letter was either in a "normal" or "reflected" orientation, and participants were required to distinguish between the two possibilities. Reaction times (RT) and percent correct choices were recorded. Though the hemisphere of input effect was not statistically significant in terms of RTs, normal participants made more errors when stimuli were presented to their RH (left hemifield). On the other hand, the LH was much faster in making correct decisions than the RH. The commisurotomized

participant showed a statistically significant advantage for the left hemifield (RH) trials in which he made considerably fewer mistakes. In contrast, in the normal sample, left hemifield (RH) presentations were responded to faster the right hemifield (LH) presentations. The authors attribute the LH superiority in the performance of the mental rotation task in normal participants to the fact that the stimuli used rotated letters. Since the LH is specialised for the processing of verbal material, this would be a likely source of the processing superiority. Fischer and Pellegrino (1988) conducted a study similar to that of Corballis and Sergent (1989) but used both uppercase alphanumeric characters and Primary Mental Abilities (PMA) characters (i.e. eight two-dimensional figures from the PMA test (Thurstone, 1958). These stimuli were presented to each visual field, and the participants were again required to identify whether they were identical or different, and to press a response key with either their left or right hand. The stimuli were rotated in the picture plane and were either "normal " or "backward" (i.e. mirror reversed). Fisher and Pellegrino found an overall LH superiority of about 20 msec across all conditions in their latency data. Since this duration is comparable to reported corpus collosum transfer time (Hoptman and Davidson, 1994), the authors suggested that the delay in processing when stimuli are presented to the RH may be due to a transfer of information to the LH which, in fact, may perform the actual rotation. The LH also made significantly fewer errors with alphanumeric characters which, in their opinion, is consistent with a LH superiority based on the phonemic processing of linguistic stimuli.

Burton et al., (1992) also reported visual field differences for the directionality of rotation. They found that clockwise rotations are performed faster in the left visual field (RH), while counter clockwise rotations were faster and more accurate in the

right visual field (LH). In this experiment, geometric line drawings were used as stimuli and were presented visually in a lateralised manner. The authors speculate that clockwise rotation, when in the left hemifield, and counter clockwise rotation, when in the right hemifield are both medially directed rotations. However, the origin of this hemifield difference in directional rotation is still unclear. As already mentioned, a number of studies do not find hemispheric differences in performance of mental rotation in either direction (Cohen and Polich, 1989)

Ratcliff (1979) tested patients with right, left and bilateral penetrating missile wounds. His task involved viewing stick-figure men holding a black disk in one hand and a white disk in the other, and judging whether the black disk was in their right or left hand. The figures were presented in four different orientations: facing the subject upright, facing the subject upside-down, facing away from the subject upright, and facing away from the subject upside-down. Ratcliff compared subjects' performance in the upright condition to their performance in the upside-down condition, which presumably involved mental rotation. He found that, whereas there were no significant differences between patient groups in performance on the upright stimuli, the right posterior group was significantly impaired on the upside-down stimuli, compared to the other brain-damaged groups and normal control subjects.

Hadano (1984) presented unilateral right and left-hemisphere-damaged patients with a variation of Cooper and Shepard's (1973) mental rotation task. Subjects were shown five versions of the same letter arrayed in a row, all at different orientations, and were instructed to mark the one letter that was mirror-reversed. Hadano found that both right- and left-hemisphere-damaged subjects were impaired in this task relative to

normal control subjects, and that there was no significant difference between the two hemispheric groups.

In conclusion, there seems to be little agreement among the outcomes of the studies reviewed above concerning the localisation of lesions causing mental rotation impairments. One reason for this may be that the mental rotation tasks used in these studies are sensitive to different aspects of the cognitive processes involved in transformation of stimuli. It is not true that any task that requires the identification or comparison of misorientated objects involves mental rotation. Indeed some have argued that the only tasks that evoke mental rotation are tasks in which misorientated stimuli must be discriminated from their mirror images (Corbetta, 1998: Hinton and Parsons, 1981). On the basis of these findings it is difficult to draw any firm conclusions about localization.

3.2.2 Neuroimaging Studies

A somewhat perplexing set of results also comes from other more neuropsysiological studies. Deutsch et al., 1988 reported greater RH than LH blood flow during rotation of Shepard and Metzler (1971) cube assemblies, while Ornstein et al., (1980) found greater LH than RH parietal activity using EEG techniques for the same stimulus materials. In Deutsch et al's., (1988) study, however, the authors compared regional blood flow (using ^{133}Xenon-inhalation technique) in four brain regions. These divisions were somewhat arbitrary as it was done in an attempt to separate association areas of the cortex from those involving primary sensory-motor functions. Curiously, three of these four regions, as divided by the authors, were comprised of both primary sensory-motor cortical areas and association areas, and this overlap makes it difficult

to interpret their finding of greater right hemisphere involvement during the mental rotation task.

A different sort of problem is encountered in the study conducted by Ornstein et al., (1980), and is a difficulty often found in other mental rotation studies as well. The problem is that no control tasks for the component processes involved in mental rotation performance were employed. More specifically, participants are asked to perform a mental rotation task and physiological or chronometric measurements were taken. However, since mental rotation is comprised of many cognitive components, it is impossible to discern which of the subcomponents may be contributing most to the registered change in regional blood flow, the reduction in alpha power, or hemispheric performance superiority. An additional difficulty in the Ornstein et al (1980) study is that recordings were taken over the parietal and central regions, thus leaving possible activation of the prefrontal areas, temporal lobes and occipital lobes unmonitored.

Even though researchers acknowledge the possibility that different hemispheres mediate different components of a mental rotation task, little attempt has been made to develop a technique that would isolate other subprocessess from mental rotation itself. One recent exception however, is the work of Cohen et al., (1996). In their fMRI study, neurologically normal individuals mentally rotated pairs of Shepard and Metzler (1971) figures into congruence, or in a comparison condition, determined if a pair of three dimensional (3D) block stimuli were identical or mirror reversed. In the latter, the authors contended that, because both stimuli of the pair appear in the same orientation, the comparison condition involves the same encoding (comparison and decision processes as the Shepard and Metzler task), but requires no mental rotation.

They further reason that by subtracting the activational profiles generated during each of these two tasks, the cortical activity specifically associated with the process of mental rotation would be revealed in relative isolation from other subcomponents comprising the task.

In their study, Cohen et al., (1996) found consistent foci of activation during mental rotation in Brodmann areas (BA) 7a and 7b (sometimes spreading to BA 40), the middle frontal gyrus (BA8) and some extrastraiate activity, including BA19 and 39 (essentially the brain regions corresponding to V5). Moreover, differential activation of the frontal cortex (BA9 and 46) was obtained, along with above threshold activity in the premotor cortex (BA6). In more than half the subjects tested, hand somatosensory cortex was engaged, and in 50% of the participants, there was an increase activation in BA18. There was little evidence of any asymmetrical lateralisation of cortical activity.

Further attempts at identifying areas involved in mental rotation were investigated by Tagaris *et al* (1996). They investigated the relationship between functional activation of the superior parietal lobule (SPL) and the performance in the Shepard-Metzler mental rotation task. This study employed the Shepard and Metzler (1971) figure in "same " and "mirror" orientations, as in pervious studies (Cohen et al., 1996). The subjects' task was to judge whether the two objects of a pair were the same or mirror images. For each object seven perspectives views were generated by a rotation in depth, around the vertical axis. Presumably to avoid any rotational or "flipping" strategy of stimuli, the control task used consisted of pairs of identical two-dimensional longitudinal rectangles. Their findings indicated increased activation in

the SPL, which correlated with increased task difficulty assigned to the encoding of visual images and the mental rotation of the figures. One surprising aspect of this study, however, is that the control or comparison condition employed 2D figure while the ON phase employed 3D figures. This fact may have an effect on the brain activation they attribute to mental rotation per se, as their resultant activational profile might reflect the combined activity of spatial encoding of a 2D and 3D object and/or mental rotation, rather than isolating the specific regions than mediate rotation as distinct from other component processes.

Alivisatos & Petrides (1997) measured regional cerebral blood flow with positron emission tomograghy (PET) during mental rotation of alphanumeric characters that were asymmetrical in both the horizontal and the vertical axes. Each one of these stimuli was presented within a circle in either its 'normal or 'backward' (i.e. 'mirror image') form. The stimuli were the upper case letters G, F, R, and the arabic numerals 2, 5. The results of this paper gave no indication of V5 activation, as reported in the Cohen et al., (1996) paper, but pointed to activation in the left inferior parietal cortex, occupying the intraparietal sulcus and the cortex below it. Significant activity was also seen within the head of the caudate nucleus.

A recent study by Kosslyn et al., (1998) compared mental rotation of cube assembly figures similar to Shephard and Metzler, (1971) and mental rotation of hand shapes. Kosslyn and colleagues compared each rotation condition to the corresponding base-line condition and then compared the two types of rotation directly. When the cube rotation condition was compared with that in the cube baseline condition, they found activation in the inferior and superior parietal lobes bilaterally. This may reflect in

part the contribution of motor processes (e.g., Milner & Goodale, 1995) and spatial attention (e.g., Posner & Petersen, 1990). They also found activation in the rotation condition in four portions of Area 19 (two in each hemisphere).

In the hands rotation condition they found activation in the left precentral gyrus, which corresponds to primary motor cortex. They also found activation in the left premotor area (Area 6), the left superior parietal lobe, two portions of the left inferior parietal lobe, left insula and left superior frontal cortex (Area 9). No activity at all was observed in the right hemisphere, which is in striking contrast to the results reported by Deutsch et al. (1988) with the Shepard-Metzler figures. Finally, Area 17 was activated along the midline. This could indicate that participants encoded more visual information in the rotation condition, or could reflect the top-down priming mechanism that may underlie rotation

When they compared which areas were more activated during hands rotation than during cubes figures rotation. They found greater activation during hands rotation in four regions of the left hemisphere: area Ml (the motor strip), Heschl's gyrus (primary auditory cortex), the insula, and dorsolateral prefrontal cortex.

V5A was recently identified using fMRI. (Haug et al., 1998). This group reported that V5A was located within the border region of occipito-temporo-parietal cortex, in four of 10 subjects on both sides, and on the right or left side in three subjects each. The stimulus they used consisted of a black-and-white sine-modulated windmill presented either stationary or in rotation phases of 1 s duration. Areas V1—V3 were not active with this paradigm. The authors also claimed that focusing attention by mentally

counting the number of rotation phases ensured high signal intensity in V5A, whereas moving attention away by counting electric stimuli to the wrist diminished it despite persistent fixation of gaze to the centre of the windmill.

3.3 Rationale and Aims

The results from all these studies suggest numerous candidates for the neural substrate of image transformation and clearly it is a complex mental activity that involves a variety of processes carried out by different regions of the brain. None of the studies have employed the appropriate reference conditions to shed light on the image transformation process, namely a perceptual task that is the same in all respects except for the cognitive process of imagery. Such a strategy has proven effective in investigations of colour imagery (Howard et al., 1998). In the present study we used functional magnetic resonance imaging (fMRI) to investigate rotational and linear transformation of stimuli. We chose to match as closely as possible perception and imagery tasks both in terms of task demands as well as "perceptual" content to minimise this problem, and carried out within subject comparisons. We were less concerned with the precise location of the different visual processes than with the potential to map the overlap between functionally equivalent perceptual and imagery tasks. We tested the following specific questions (i) Can V5 or similar regions be reliably activated by the perception of both linear and rotational motion? (ii) Are the same regions activated by imagery of linear and rotational transformations of the same stimuli? To investigate these questions functional magnetic imaging was used to measure localised changes in blood oxygenation during both perception and imagery in the same subjects in the same session.

3.4 Methods

3.4.1 Subjects

Six normal healthy volunteers between the age range 23-40 were recruited from the staff and students at the Institute of Psychiatry. They gave their informed consent and were free from any contraindications that prevent scanning. Demographic details are given in table 3.1

Table 3.1
Subject Demographics

SUBJECT NUMBER	GENDER	HANDEDNESS	AGE
1	M	R	39
2	M	R	40
3	F	R	23
4	F	R	30
5	M	R	35
6	M	R	37

Prior to scanning all subjects were given full instructions before entering the scanner. For both experiments subjects were trained with a set of practice trials to allow them to experience the task outside the scanner. For the imagery conditions all subjects reported that they used internal imagery to make their comparisons.

3.4.2 Experimental design and procedure

During the investigation the stimuli were projected by a computer controlled projector system onto a screen placed across the bore of the magnet 1.8 metres from the subjects' eyes, and viewed by subjects through a prismatic mirror. An ABAB design with 5 repeats of 30-sec presentation of ON and OFF phases of each paradigm was

employed beginning with the ON phase. The following explanations of the stimuli are show graphically in figure 3.1

Stimulus for perception of rotational motion

The stimuli in the rotation experiment comprised of 12 cube assemblies similar to those used by Shepard and Metzler (1971). The stimuli were created using Quick Basic programming language and displayed on a personal computer. Figure pairs were created from these cube assemblies. In the ON phase subjects viewed stimuli which changed every 10 secs, one of which rotated at a speed of 270 degrees per sec. The position of the rotating figure was pseudo-randomised so there was equal number rotating on the right side as the left side of the display. In the OFF phase subjects viewed the same pairs of figures, but both were stationary. The stimulus ordering was pseudo-randomised, so that each of the figures appeared once before another figure appeared twice, and each figure appeared twice before any other one appeared three times, etc. The figures for the trials were split so that half were mirror image figure and half were identical (see table 3.2)

Table 3.2
Summary of paradigm for the perception of rotation motion

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Cube-assemblies, one of which was rotating	Watch rotating cube-assembly
OFF	Stationary cube assemblies	Decide whether the two cube-assemblies are identical or mirror images

Stimuli for mental rotation

In both the OFF and ON phases subjects viewed similar Shepard and Metzler figures which changed every 10 secs. The subjects were asked to look at each pair, and to decide whether the pair of figure were identical or mirror images and to indicate their choice by pressing one of two buttons using either their left or right index finger. In the ON phase they were told to visualise the figure rotating until it aligned with the other figure, and then to decide whether the two figures were identical or mirror images of each other. Again the subjects were to make a response by pressing the appropriate button (see table 3.3)

Table 3.3
Summary of paradigm for mental rotation

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Cube-assemblies- one of which was offset	Mentally rotate the cube assemblies into congruence and decide whether the two cube-assemblies are identical or mirror images
OFF	Stationary cube assemblies	Decide whether the two cube-assemblies are identical or mirror images

Stimuli for perception of linear motion

In the ON phase subjects viewed a pictorial representation of a stationary target with an arrow moving horizontally and "hitting" the target. This was displayed for 3secs, followed by a 2sec gap before the next arrow appeared. The arrow "hit" the target on the "bull's eye" or "outside the bull's eye". The subjects' task was to decide whether

the arrow "hit" or "missed" the "bull's eye" by pressing the appropriate button as quickly and accurately as possible. The OFF phase consisted of the same stimuli without the motion content. In this phase the arrow was already positioned on the target and the subjects task was to indicate if the arrow was in the or outside the "bull's eye". The position of the arrow was randomised with equal numbers pointing left and right. There were an equal number of hits and misses (see table 3.4).

Table 3.4
Summary of paradigm for the imagery of linear motion

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Arrow moving towards stationary target	Decide whether the arrow hits the "bulls-eye" of the target
OFF	Stationary target and arrow	Decide whether the arrow is in the "bulls-eye" of the target

Stimuli for linear transformation

In the ON phase a target and an arrow appeared every 3 secs followed by a 2 secs gap. The arrow was placed on either side at the edge of the subjects visual field pointing towards the target. Subjects were told to "move the arrow mentally" towards the target and to make a decision as to whether the arrow hit or missed the "bull's eye" via a button press as before. The OFF phase was identical to the OFF phase in the linear motion perception task (see table 3.5)

Table 3.5
Summary of paradigm for linear transformation

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Arrow pointing towards stationary target	Mentally move the arrow towards the target and decide whether the arrow hits the "bulls-eye" of the target
OFF	Stationary target and arrow	Decide whether the arrow is in the "bulls-eye" of the target

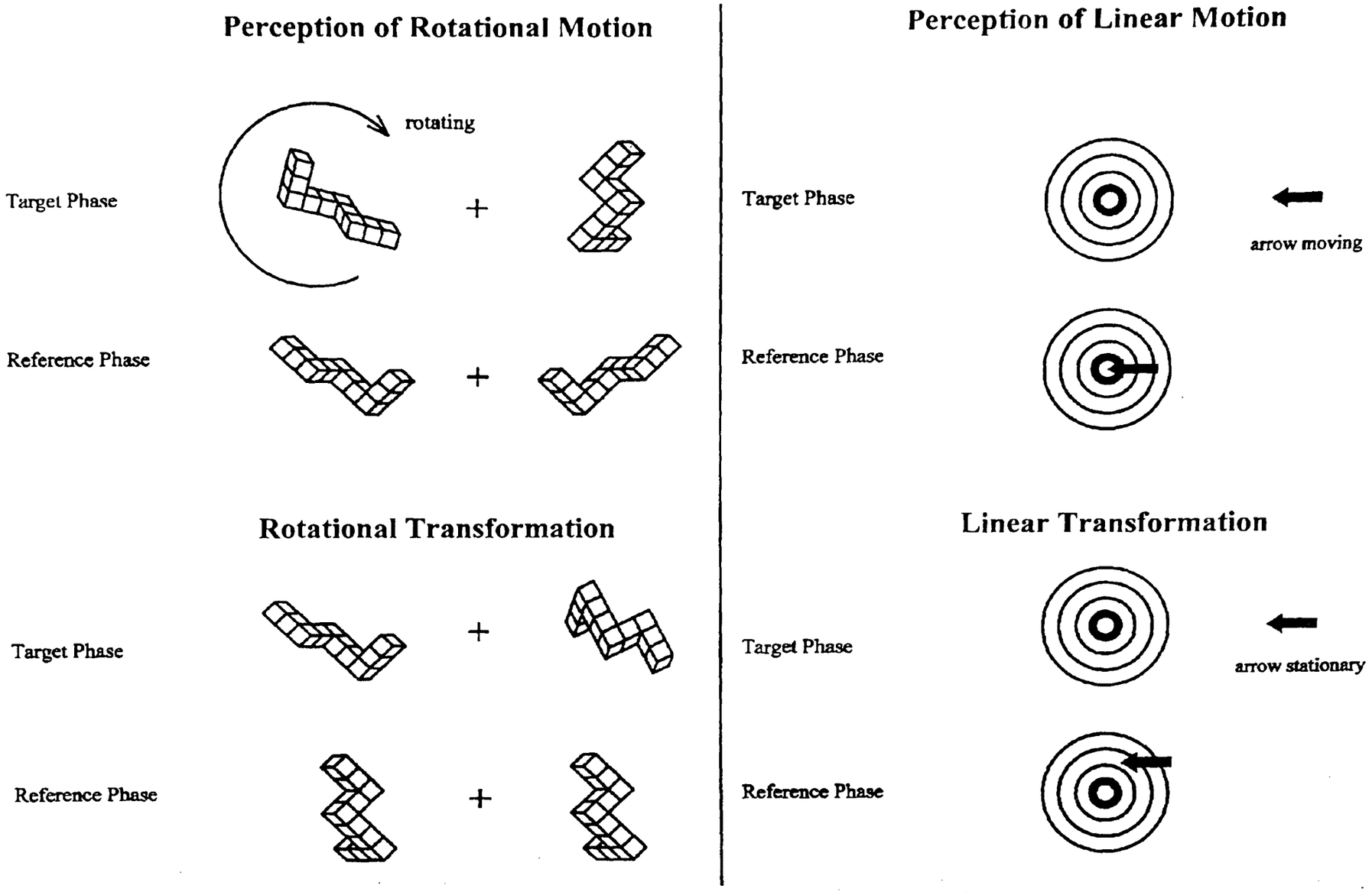


Fig. 3.1 Examples of stimuli used in the experiments. In the Target phases (ON condition) of both experiment subjects viewed the stimuli in motion. In the reference phase (OFF condition) the stimuli was stationary and subjects were told to mentally move the stimuli

3.5 Behavioural Results

We recorded response times on-line for the rotational transformation task. This allowed us to determine the behavioural pattern of the mental rotation process. Response times were also collected in the linear tasks however, the distance of the "arrow" to the target was the same throughout the imagery task. The response time for rotational transformation was submitted to a paired sample t test. Only those times from the trials when subjects made a correct response were analysed. Outliers were eliminated prior to analyses (>2SDs). In all subjects, the response time increased appropriately with the angular disparity (see figure 3.2). A paired sample t test confirmed that (i) subjects required more time in the rotation condition than the control condition $t = -54.007$, $p<.001$ and (ii) a Pearson correlation revealed an angle-reaction time correlation of 0.913, significant at the 0.01 level.

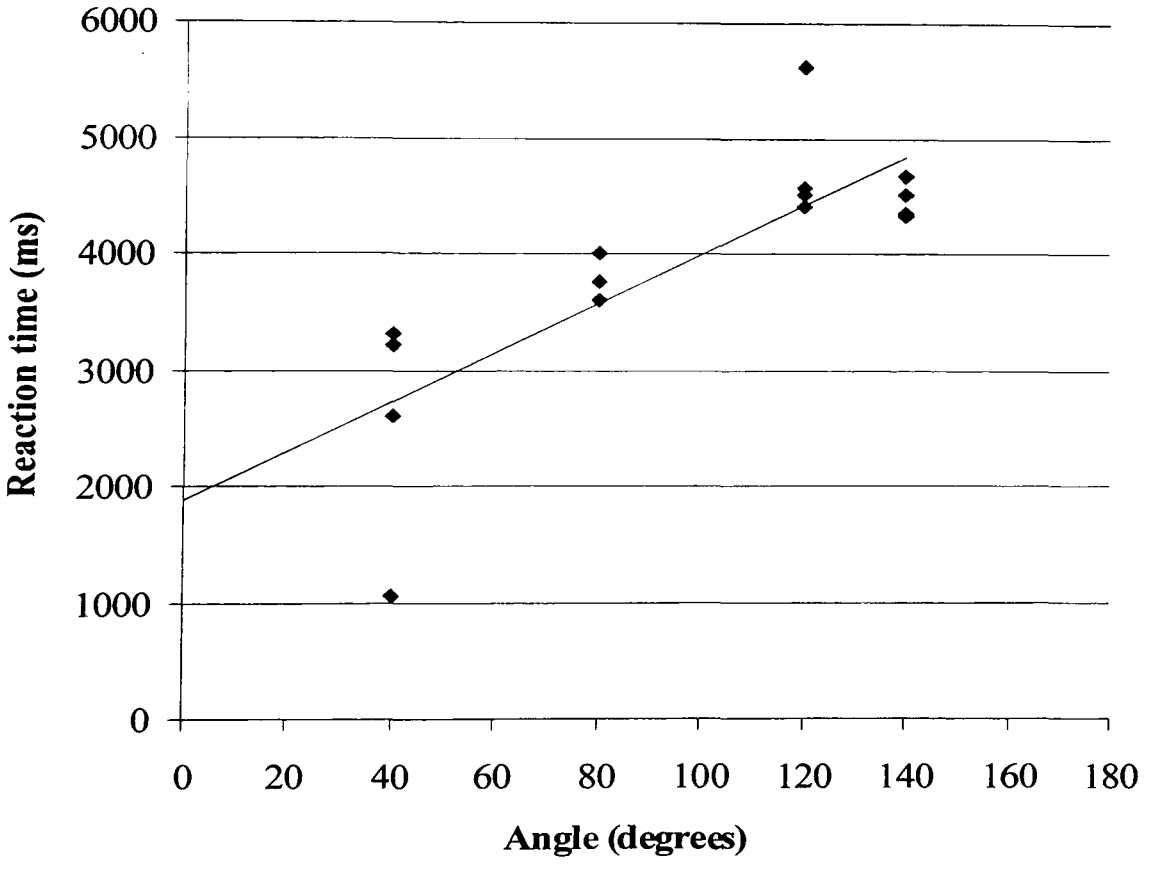


Figure 3.2.
Graph showing a linear increase in reaction times with angular disparity in the mental rotation task

3.6 Neuroimaging Results

3.6.1 Perception of rotational motion (figure 3.3)

The most extensive areas of activation during rotation motion perception were in the angular gyrus, though more pronounced to the left (see table 3.6). Activation of the ventrolateral occiptotemporal junction or V5 (BA39/19) was also observed in both hemispheres. Areas of primary visual cortex activation were evident in the left hemisphere, but did not extend to the right hemisphere. Activations were also detected in the right precuneus and small but significant bilateral activation was evident in the precentral gyrus.

3.6.2 Rotational transformation (figure 3.3)

According to post experimental reports all subjects reported using mental imagery in the ON phase. Imagery of rotational motion elicited substantial activation in a number of different brain regions. The most widespread clusters localised to the left Brodmann area 19 and superior parietal lobe, the left premotor and the supplementary motor area (SMA) and the precuneus in both hemispheres. Small activations were evident in the primary visual cortex and the inferior temporal gyrus in the left hemisphere (see table 3).

Table 3.6
Major regional foci of activation when subjects ***viewed rotational motion*** against reference condition ($p<0.0002$)

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Angular Gyrus	-43	-64	15	40
Area V5	-40	-64	9	35
Area V5	-40	-67	4	11
Precentral Gyrus (M1)	-35	-33	48	3
Premotor & SMA	-3	3	53	2
Primary Visual Cortex V1/V2	-9	-81	4	2
Right Hemisphere Regions				
Area V5	46	-61	9	39
Area V5	46	-64	4	20
Angular Gyrus	46	-61	15	19
Precuneus	6	-47	53	10
Inferior Temporal Gyrus	38	-69	-2	5
Precentral Gyrus (M1)	35	-33	48	3

Table 3.7
Major regional foci of activation for ***rotational transformation*** against reference condition. ($p<0.0002$)

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Precuneus	-17	-64	53	28
Area 19	-26	-72	31	15
Superior Parietal Lobe	-40	-39	59	17
Premotor and SMA	-43	0	42	8
Precentral Gyrus	-46	-22	42	5
Primary Visual Cortex V1/V2	-9	-83	4	2
Right Hemisphere Regions				
Precuneus	17	-61	59	11
Area 19	26	-75	31	3
Inferior Temporal Gyrus	38	-61	-2	3

3.6.3 Perception of linear motion (figure 3.4)

Overall activation was less for the perception of linear motion when compared to its rotational counterpart. Significant activations were detected in the supermarginal gyrus and angular gyrus in the left hemisphere (see table 3.8). Activation of area V5 was small and only occured in the right hemisphere, but did extend across two contiguous slices. Activation was also evident in the middle temporal gyrus and precuneus in the right hemisphere.

3.6.4 Linear transformation (figure 3.4)

There was no evidence of such wide spread activation of V5 when comparing either imagery task with its reference task, although activation within the primary visual cortex was observed (see table 3.9). The main foci of activations were detected in the precunues of both hemispheres. Activation of area 19 was also observed in both hemispheres.

Table 3.8
Major regional foci of activation when subjects ***viewed linear motion*** against reference condition ($p<0.0002$)

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Supermarginal Gyrus	-40	-31	26	7
Angular Gyrus	-40	-69	15	4
Right Hemisphere Regions				
Middle Temporal Gyrus	55	-47	4	14
Precuneus	6	-58	42	11
Area V5	43	-61	9	4
Area V5	49	-64	4	4
Premotor & SMA	43	6	37	3

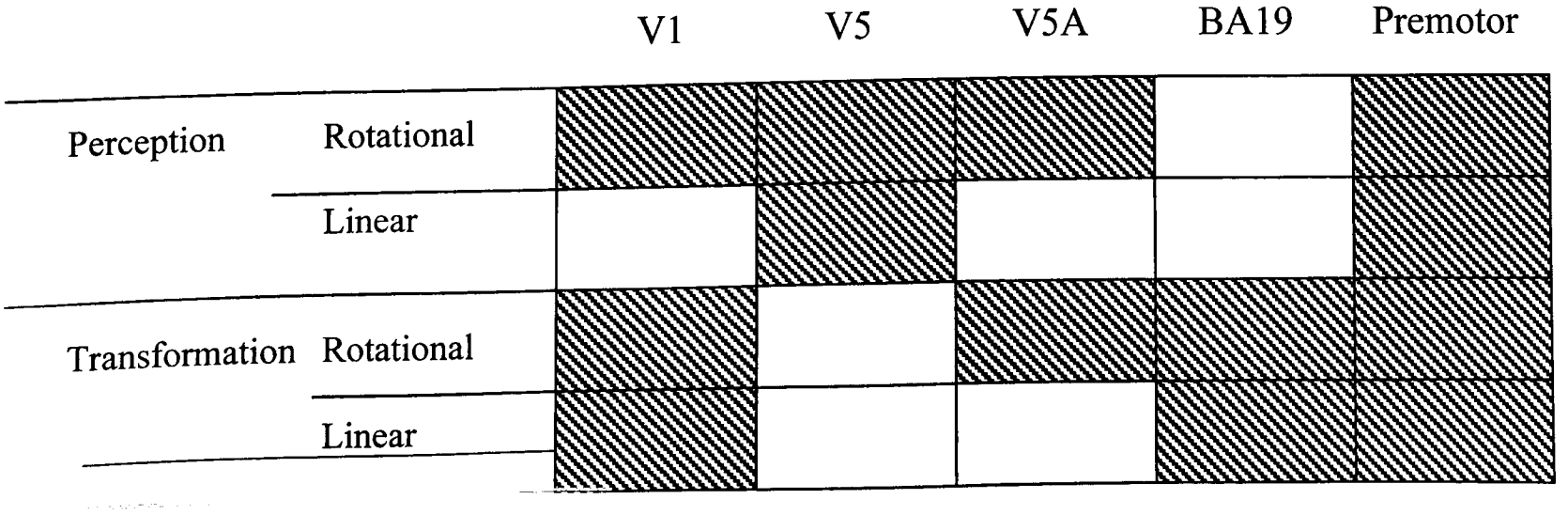
Table 3.9
Major regional foci of activation for ***linear transformation*** against reference condition ($p<0.0002$).

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Precuneus	-6	-58	37	10
Area 19	-17	-75	31	6
Precentral Gyrus	-52	0	37	3
Right Hemisphere Regions				
Precuneus	6	-58	42	11
Area 19	23	-75	31	9
Premotor & SMA	49	8	31	4
Primary Visual Cortex V1/V2	12	-75	9	4
Midline				
Precuneus	0	-53	31	9

3.6.5 Comparison of perceptual and imaginal networks

Analysis of the data sets showed small areas of activation in very close relation to each other for both the perception of rotation and mental rotation tasks (see tables 3.6 & 3.7). The location of this area in the right inferior temporal gyrus (BA19) suggested it to be V5A. In both rotational imagery and linear imagery, an increase in the fMRI BOLD signal was seen within the parietal cortex (BA19) and the primary visual cortex V1 (see tables 3.8 & 3.9). A summary of these results is given in table 3.10

Table 3.10
Summary of cortical areas activated in perception and transformation of motion
(Shading = activation)



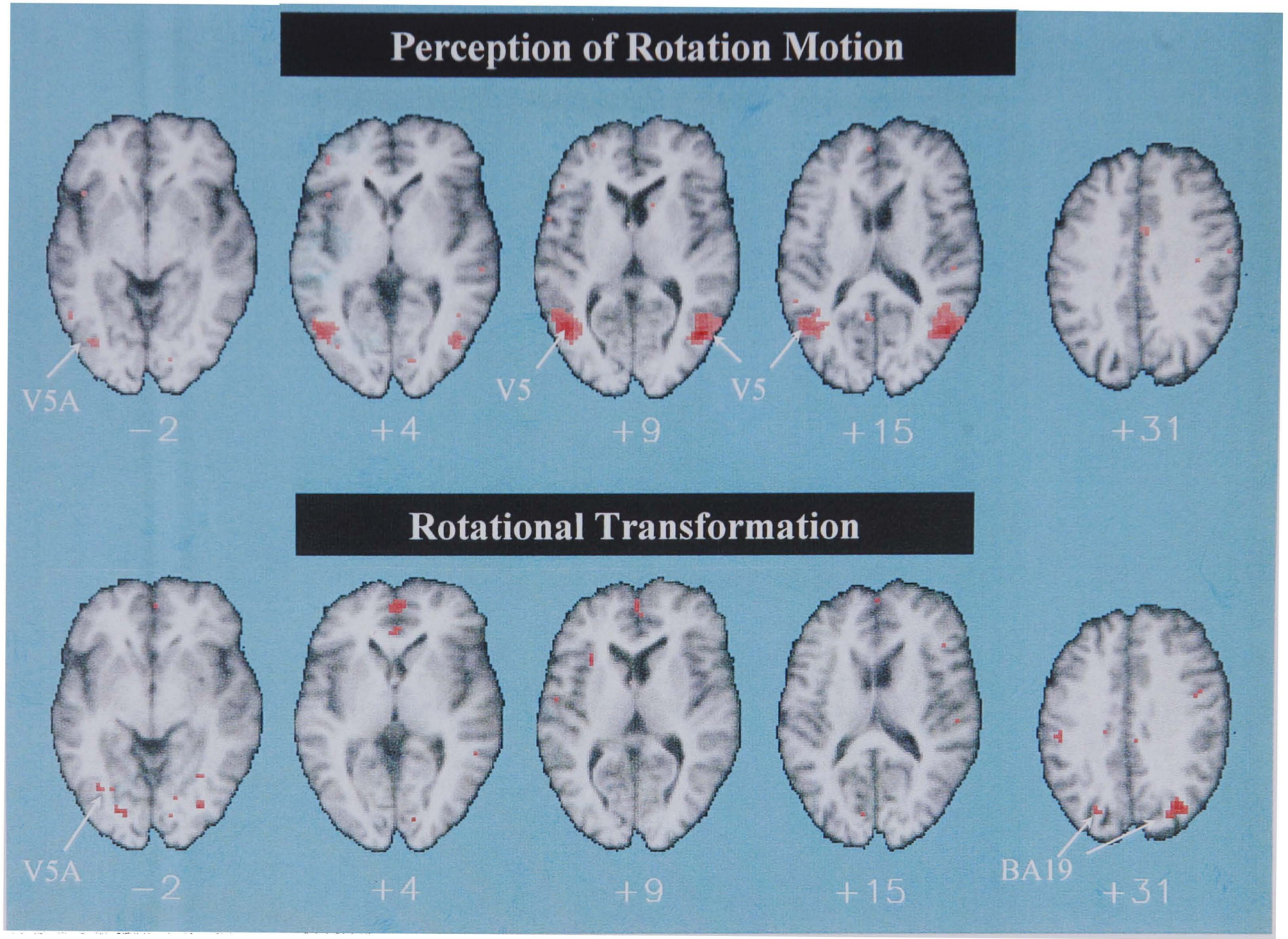


Fig.3.3 Perception of Rotational Motion and Rotational Transformation: Median generic brain activation maps (GBAMs) of activated voxels (in red) registered in the space of an individual grey scale high-resolution EPI dataset. Activation in area V5 for the perception of rotation motion was seen in both hemispheres (maximum FPQs, right: 46 –61 9; left: -40 –64 15). An activated area inferior to V5 in the dorsoventral (z) axis was evident in both perception (right: 38 –69 -2) and imagery tasks (right: 38 –61 –2). Imagery also activated BA19 (right: 26 –75 31; left: -26 –72 31)

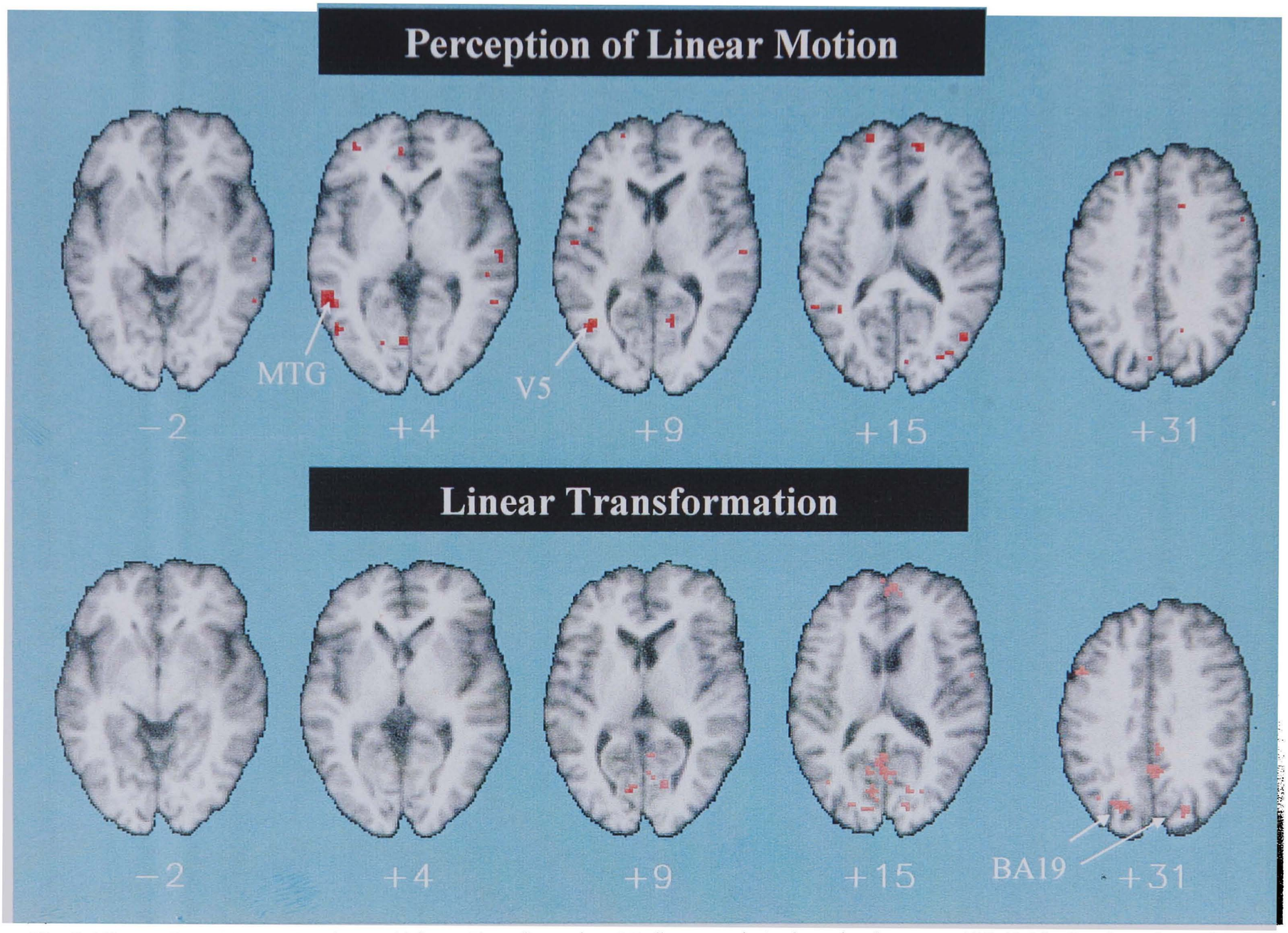


Fig. 3.4 Perception of Linear Motion and Linear Transformation: Median generic brain activation maps (GBAMs) of activated voxels (in red) registered in the space of an individual grey scale high-resolution EPI dataset. Activation in area V5 for the perception of linear motion was seen in the right visual cortex (43 -61 9). Imagery of linear motion activated BA19 bilaterally (right: 23 –75 31; left: -17 –75 31)

3.7 Discussion

The direct comparison of perceptual and imaginal cortical networks was made possible in this study by scanning each individual performing both tasks in the same session. It should also be noted that the raw visual input was balanced across ON and OFF phases of both linear and rotational experiments, although there was no condition where subject viewed displacement without motion.The primary aim of this study was to localise the brain regions involved in rotational and linear transformation. A second goal was to identify possible sites of convergence of these processes.

The perception of the visual attribute of motion in the rotation and linear conditions was associated with activity in the visual area V5 as described by previous studies (Zeki, 1991). Transformations of the stimuli resulted in a different pattern of activity; the most striking difference being the lack of activity in the large areas of V5 activated in the perception task. While the involvement of V5 is predicted during the viewing of movement, the lack of activation in this area during the mental rotation of same stimuli suggests that other areas may be specialised for image transformations. Activation was also seen in the precentral gyrus (M1) for both rotational tasks and linear transformation. Previous evidence showed this area to be active during the mental rotation of hand shapes (Kosslyn et al., 1998). However, no comparison perception task was undertaken, so whether the same area was activated for the viewing of rotating hands is not known.

Situated between the occipital and temporal lobes, the angular gyrus is a strong candidate for the functional link between the visual association cortex and memory areas in the temporal gyrus. The involvement of the angular gyrus has been seen in

the perceiving of aversive stimuli (Kosslyn et al., 1996), and visuospatial learning (Kawashima et al., 1995). These studies have suggested that the angular gyrus may be involved in the mapping of visual presented inputs and visual identification of objects. The contribution of the angular gyrus to perception of motion has been implicated in the perception of coherent motion (Howard et al., 1996) although the functional nature of its involvement remains to be specified.

The investigator was aware that eye movements made by subjects during the tasks may have lead to unwanted activation in the primary cortex (BA17), the precentral and posterior medial frontal gyrus (frontal eye field) or the medial part of the superior gyrus (supplementary eye fields) (Bodis-Wollner et al., 1997). Only minor activations were observed in the primary visual cortex and no activation was evident in the prefrontal or frontal eye fields. Activation in V1 has previously been put down to the encoding of more visual information or the influence of "top down" priming mechanisms (Kosslyn et al., 1998) and supports the view that the primary visual cortex is involved in visual imagery (Kosslyn et al., 1995). Quite divergent results have been reported by several other investigators who did not find V1 involvement during a variety of mental imagery tasks (see Roland & Gulyas, 1994). Because of such divergent results reported in the literature, the debate on the exact role of V1 in mental imagery remains open. There is, however, a general consensus that methodological issues such as sensitivity, data analysis strategies, and control task choice are unlikely to resolve the controversy in themselves alone. Rather, investigators must try to define more precisely the type of mental imagery tasks that activate the V1.

Activation of the precuneus was evident in both transformation tasks. Mental imagery is one of the major components of episodic memory recall (Tulving, 1983) and numerous studies have reported precuneus activation during episodic memory recall (Tulving et al., 1994; Andreasen et al, 1995a,b; Fink et al., 1996). In the imagery domain, the precuneus seems to be specifically recruited whenever the generation of the mental image relies on the reactivation of a memorized percept (Kosslyn et al., 1993; Mellet et al., 1995; Roland & Gulyas, 1995). The precuneus is also specifically activated by the perception of degraded images of objects or faces previously seen in an undegraded version, emphasising the role of this area in facilitating recognition by the use of previously stored information (Dolan et al., 1997). However, it is still unclear whether this region is specific for the visual component of memory retrieval (Fletcher et al., 1995) or is independent of this process. In this study both processes were taking place; the maintenance and retrieval of previously seen stimuli and the imagery of stimuli to complete the different task demands. Thus, together with previous finding the precunueus appears to be a common area for mental imagery and visual memory recall.

The mental rotation task being a three-dimension rotation was probably the most computationally demanding task in terms of rearranging the spatial location of an object although reaction times were similar in the two imagery conditions. It is not surprising therefore, that activation of the superior parietal lobe was evident in this task as it has previously been implicated in tasks involving spatial attention (Posner & Petersen, 1990), spatial localisation (Haxby et al., 1991a) and mental rotation in a similar imagery task (Tagaris et al., 1996). The lack of activation of this area in the linear transformation task may be a result of subjects viewing motion in only two

planes. In addition to this we found strong bilateral activation of BA19 which was present during both imagery tasks but not the equivalent perception tasks. This suggests it has a key role in image transformations and is consistent with previously described mental rotation neuroimaging studies (Cohen et al., 1996; Kosslyn et al., 1998).

The activation evident in the right middle temporal gyrus (MTG) was both unexpected and intriguing. Previous research has implicated this region in the storage and recognition of visual input (Kosslyn et al., 1994), and the labelling of emotional facial expressions (Rapcsak et al., 1993). Its activity in relation to the moving as opposed to the static arrow is unclear.

Most of the literature on the neural basis of image transformation focuses on the relative contributions of the cerebral hemispheres. Hemispheric asymmetry in this present study was inconclusive, however activations were larger in the left hemisphere during the mental rotation task in the precuneus and area 19. This is consistent with the finding that patients with left-hemisphere brain damage may have selective difficulty in performing mental rotation, relative to other imagery tasks (Kosslyn, 1994).

Previous literature on the lateralisation of image transformation is very complex and no simple conclusions are forthcoming. One reason for this may be that mental image transformations activate a number of subsystems depending on the transformation being carried out. Right hemisphere superiority for mental image rotation is consistent with results from studies of focal lesion patients (Butters et al., 1970; Ditunno &

Mann 1990; Ratcliff, 1979). Ditunno & Mann (1990) found that right-hemisphere damaged patients made more errors and took longer to evaluate stimuli similar to that used in this study than left hemisphere damaged patients. However, the picture is not as clear as it first appears. Mehta & Newcombe (1991) showed left hemisphere damaged patients have a deficit in rotating three-dimensional objects. One reason for much of this discrepancy in the literature is that in some cases the tasks may have tested mental rotation and other abilities simultaneously, or the tasks may have not have tested mental rotation ability at all. Indeed, it has been argued that the only tasks which reliably evoke mental rotation are tasks in which misorientated stimuli must be discriminated from their mirror-images (Corballis, 1988). Here the stimuli for mental rotation were constructed to meet these requirements and greater activation was observed in the left hemisphere. However, no such lateralisation was seen in the linear motion experiment. So, although we posit both tasks are motion-encoded transformations, different areas of the human brain were activated in each transformation. This highlights the issue of many subsystems being involved in different aspects of image transformations. Unfortunately, from these data the relative contribution from each brain region on each aspect to imagery cannot be established and as such it does seem difficult to conclude the exclusive participation of either one of the hemispheres in any of the imagery tasks.

It has previously been shown that one feature of the V5 complex is its intra-regional subspecialisation (Howard et al., 1996). It has been suggested from primate work that V5 is surrounded by satellite areas designated as V5A (Tanaka & Saito, 1989) and within this region exist cells specific to rotational (circular) motion (Andersen et al., 1990). The small areas of activation we found could be a subdivision of the V5A,

which as in monkey MST respond to more complex movements and have larger receptive fields (Andersen et al., 1990). In a recent study of "illusory" motion (Zeki et al., 1993b) it was observed that the focus activated when subject experienced "illusory" motion was located in the same sulcus as V5 in 10 out of 14 "hemispheres". In the other four hemispheres, activation was found in a sulcus lying slightly more posteriorly. The separation between the illusory and actual motion foci was taken to imply the existence of motion-related cortex , labelled V5A, immediately neighbouring V5.

The scatter of foci related to speed discrimination, identified by Corbetta et al., 1991, also suggest that the motion -related cortex goes beyond V5 in the lateral occipital gyri. The rotation component of both tasks thus utilise a subdivision of V5A close to an area previously described as critical to the perception of illusory circular motion (Zeki et al., 1993b) and rotating visual stimuli (Haug et al., 1996). Whether the foci of rotational qualities of stimuli we describe here are anatomically distinct from linear qualities, or devoted exclusively to mental rotation, is a matter for future classification.

Implications for Models of Mental Imagery

The results here underline the notion that imagery of motion is not a simple process, as is evident in attempts to develop precise models of mental rotation (see Kosslyn, 1994). Understanding the contributions of different operations to the overall process requires additional experimental evidence. The goals of this study were more modest: to explore the two different types of motion imagery and observe which brain regions are recruited. In these terms this study has demonstrated the specificity of the motion

responsive cortical areas in both imagery and perceptual tasks and further, that the neuropsychological mechanisms that underlie image transformation are dependent on the stimuli. Here we assumed the mental manipulations of the presented stimuli relied on the activation of previously stored representations of the object in motion. This appears to rely upon some contribution from motor output networks. Subjects were exposed to the stimuli moving in practise and perception phases of the experiments and thus, were able to encode and store the moving stimuli in a "pattern activation subsystem" at different points in time (Kosslyn, 1994), which could later be visualised in the imagery conditions. This has been referred to as a motion-encoded transformation (Kosslyn, 1994). If the stimuli had only been seen in a static condition as in previous work (Cohen et al., 1996), the subject could not simply "play back" previously encoded moving images but would have to "add" the motion to the object in the mind's eye. Both transformations it would seem, are a combination of visual and motor processes, but only motion encoding may lead to the involvement of the motor and premotor areas. While our behavioural data do not address this issue directly, we would predict based on previous work (Kosslyn, 1994) that motion-encoded transformation would elicit quicker reaction times.

3.8 Conclusions

In summary this study has shown that altering the nature of visual transformation, linear versus axial results in different areas of the human cerebral cortex being activated (see table 3.9). Decomposition of these task elements enabled us to reveal functional specialisation within both visual imagery and perceptual systems. What is also evident from this study, is that in moving towards specifying a model of image transformation, care must be taken to consider the type of stimuli being manipulated.

Chapter 4: The Functional Anatomy of Imaging and Perceiving Colour.

Howard, ffytche, Barnes et al., (1998) The Functional Anatomy of Imaging and Perceiving Colour.*NeuroReport* 9, 1019-1023

4.1 Introduction

As detailed in chapter one, visual imagery occurs when visual information is retained or when stored visual information is activated, creating a short-term memory representation that is accompanied by experience of "seeing with the mind's eye" (Kosslyn 1994).Visual agnosia is frequently accompanied by the loss of visual imagery (Davidoff & Wilson, 1985; Levine et al., 1985; Taylor & Warrington, 1971). Loss of spatial organisation in visual perception has also been found to accompany an equally selective imagery deficit (Levine et al. 1985) These early studies on normal and brain damaged individuals reinforce the view that visual imagery and visual perception are mediated by a common neural substrate and activate the same representations (for review see Farah, 1984; Farah, 1988). Thus, one should expect selective deficits in the imagery abilities of patients that parallel their selective perceptual deficits. In this article we will examine the visual submodality of colour and outline what is known about the cerebral localization of colour imagery. Neuropsychological studies of colour imagery that are of direct relevance to the debate will be reviewed. Space will then be devoted to neuroimaging studies of colour imagery. Both the techinques of PET and fMRI will be discussed in terms of the light they shed on the neural substrate of colour imagery.

4.2 Literature Review.

In the visual system, colour is represented as a separate module from other properties of a visual stimulus. This modular input theory requires that brain damage could

completely remove colour vision yet leave all other visual functions intact. The association between loss of colour perception and colour imagery has been observed in a number of case and group studies and has lead some authors (Farah, 1988; Damasio, 1989) to advocate that colour is represented by the same neural structures in imagery and perception. Farah (1988) considered a number of findings from neuropsychology and concluded that there were three types of evidence that support the idea that imaging an object in colour requires some of the same neural representations needed for colour vision (1) the long history of individual cases with acquired achromatopsia who have lost colour imagery, (2) both images and visual representations are equivalent in terms of their interactions with other visual and verbal task components and, (3) that colour imagery correlates with colour vision in a group of patients with varying degree of colour vision impairment. Evidence of the association between colour perception and colour imagery has a long history (e.g Damasio et al., 1980; Gomori & Hawryluk 1984; Levine et al., 1985; Humphreys and Riddoch, 1987; Rizzo et al., 1993; Goldenberg, 1992).

Levine et al.,1985 (case 1) described a patient with cerebral achromatopsia following a road traffic accident. The patient's comments and performance on colour discrimination and colour matching suggested a perceptual disorder. The patient also had difficulty describing colours of objects from memory, which appeared to be due to problems with imagery as descriptions were aided if the object had a strong colour association. The inability to visualise colour was also detailed in a study by Humphreys and Riddoch (1987). Here a colour-blind patient with good general imagery ability performed well when drawing or describing objects from memory. However, he had a colour perception deficit and the ability to image in colour was

absent. Evidence cited to support this hypothesis comes from single case studies by Damasio et al., (1980 case 2). The patient is reported to have had complete acromatopsia with defective colour matching and colour naming. Visual imagery was reported to be colourless, but intriguingly, dreams were in full colour. So, although one could argue that the neural structure that represents perception and imagery to be the same, as deficits in these cases may be seen in both domains. Some mechanisms required for colour perception may not be needed for colour imagery, since colour was present in the dream state.

As well as single case studies, DeRenzi and Spinnler (1967) carried out a group study of colour-related impairments on patients with unilateral brain damage. Colour vision was assessed by first having the patient sort a set of coloured paper squares into pairs having the same colour and second, by having the patient complete the Ishihara test of colour blindness. Imagery also was tested in two ways; by asking the patients question such as "What colour is a tangerine?" and by having patients colour black and white line drawings with a colour of their choise. DeRenzi and Spinnler found that when patients had a colour perception deficit, they also showed impairment on the visual imagery tasks. These patients had perceptual deficits on colour matching and Ishihara plates after right posterior lesions. Errors in stating the colour of objects from memory or in colouring drawings were also seen. This held true when patients with no memory or language impairment were required to state the colour of objects from memory. On what was believed to be an adequate test of colour imagery, the patients with colour perception problems had difficulty in selecting the correct colour to colour a black and white drawing.

Considering the verbal-verbal colour memory task for assessing colour recall, the verbal requests for the colour of objects could have been arrived at in two ways. The patient could have generated an image in the mind's eye and inspected the colour before giving their answer, or alternatively they could have relied on verbal colour-object associations which are totally separate from the process of imagery. The patient in performing the task has therefore no need to generate the object and the failure to arrive at the correct colour could be due to incorrect colour-object association. It is therefore difficult to determine whether the errors that occur are due solely to a colour imagery deficit. However, the authors concluded that there is "a close relationship between colour perception and colour revisualization".

Verbal-paired association recall is shown in the study by Rizzo et al., (1993). Both patients in this study could recall the appropriate colour name associated with most items in a list of objects because the names of the objects are strongly associated with their colour. However, on the few items that are infrequently paired with colours (eg lead), the subjects had difficulty in correctly responding as they had to rely on recalling the items colour from long term visual memory.

Despite the abundant evidence for a considerable overlap in the neural structures of colour perception and imagery in that colour revisualisation impairment is almost always present in patients with impaired colour perception, this association is far from being the rule. Reports are coming to light that suggest the neural structures of these systems are not identical and that the deficits seen in colour perception are not always paralleled in colour imagery. Patients have been described with impaired mental

colour imagery and preserved colour perception, suggesting a possible imagery deficit (Stengel, 1948 case 1; Farah et al., 1988; DeVreese, 1991)

De Vreese, 1991 reported a patient (M.A) with bilateral extrastriate lesions who showed preserved colour perception but impaired colour imagery. This patient could no longer recognise or evoke visually presented colours of objects when she was prevented from relying on her verbal knowledge of colours. She said she could picture anything except colours although she continued to see and discriminate colours. She also had difficulty answering questions about hue, requiring visual imagery

Perceptual and imagery deficits can dissociate one from another in several domains. Visual imagery can be spared in cases object agnosia (Behnmann, et al., 1992; Servos and Goodale, 1995). and of cortical blindness (Chatterjee & Southwood, 1985; Goldenberg et al., 1995). A colour perceptual deficit with intact colour imagery has also been reported (Shuren et al., 1996; Bartolomeo et al., 1997; Bartolomeo et al., 1998)

Bartolomeo et al (1997) reported the case of a 74-yr-old female patient who, after sequential bilateral strokes in the occipital regions, sparing the primary visual cortex, developed a severe deficit of colour perception. To investigate colour perception, she was tested on colour discrimination, matching, pointing and naming tasks. Colour imagery tasks consisted of colour verbal memory, colour-object fluency (De Vreese, 1988), colour name fluency (De Vreese 1991) and mental hue comparison tests. Although she showed severe deficits in the colour perception tasks she had perfectly vivid visual imagery for colours. This same dissociation of intact colour imagery with

severe achromatopsia was reported by the same group in a later study of a patient with bilateral brain lesions in the temporo-occipital cortex (Bartolomeo et al., 1998)

Shuren et al., (1996) examined the colour perception and imagery of a 63-yr-old male with achromatopsia secondary to bilateral temporo-occipital infarcts inclusive of the lingual and fusiform gyri. As with the previous study, neuropsychological testing revealed that the patient had impaired colour perception and an inability to name viewed colours. However, he had preserved colour imagery and colour naming of visually imaged colours.

These studies challenge the theories which posit that the same cognitive processes are involved in both the perception and the retrieval from memory of a given stimulus. However, as discussed earlier, visual imagery deficits more often mirror visual perceptual deficits in the same domain (see chapter 1.) This has lead some to suggest a common neural substrate for perception and imagery (Damsaio, 1989; Farah, 1988, 1989; Kosslyn, 1994) with domain-specific cortical areas being used to process the same kind of information in perception and retrieval from memory.

In Kosslyn's (1994) model, colour perception and colour imagery share a common visual buffer, in which both mental and physical colour percepts occur. The image generation process occurs by the content of long-term memory being transferred onto this visual buffer. Thus, a selective deficit of the generation process should result in impaired imagery. If as Kosslyn (1994) states the visual buffer is a structure in the occipital lobe, composed of retinotopically organised areas from VI to V4 that constitutes the common "screen" for perceptual and imagery processes, a reasonable

assumption would be that the functional locus of impairment in these cases is at the level of the visual buffer. Moreover, if memory contents are retrieved through the retroactivation of the very same cortical areas that had processed the relevant information during perception (Dasmassio's 1989), the lack of visual imagery of colour could be explained either by direct damage to a cortical area specialised for colour processing (V4), or by a disconnection of V4 from primary visual areas (V1). Neither of these accounts explain the apparent dissociation between imagery and perception though.

Kosslyn (1994), argues that dissociation in imagery and perception can be accommodated by his model. In Kosslyn's own words, "problems in perceptual organisation or in matching input to stored visual representations in the pattern activation subsystems can impair perception but leave imagery relatively intact (pg. 329)". However, the imagery ability of individuals in some of these patient studies are not *relatively spared* but appears vivid and appears fully intact.

In a PET experiment (Martin et al., 1995), subjects had to generate the name of colours associated with an achromatic line drawing of an object, or with its written name. In both conditions, a region in the ventral temporal lobe was activated anterior to the region of the fusiform gyrus activated by colour perception (Zeki et al., 1993a), suggesting distinct cortical regions in the perception and imagery of colours. However, although this result at first seems to support an anatomical distinction between colour perception and colour knowledge, the cortical regions that mediate colour perception were not identified in that study. Also, the colour information retrieval condition was compared with a baseline task of naming achromatic objects,

that has been shown to elicit occipital cortex activity (Bookheimer et al., 1995; Kiyosawa et al., 1996; Martin et al., 1996). Therefore, the results of the colour retrieval condition could have been confounded when comparing it with an object-naming baseline. However, the fact that these cortical areas appear to lie so close to one another would make them liable to be damaged as the same time, thus accounting for the frequent observation of an association between perceptual and imagery deficits in colour processing.

4.3 Rationale and Aims

To further explore the similarities and differences between perceptual and imaginal networks within the submodality of colour we used the technique of fMRI to map the cortical areas activated when subjects viewed or were asked to imagine colours.

4.4 Method

4.4.1 Subjects

Seven normal healthy volunteers recruited from the staff and students at the Institute of Psychiatry between the age range 23-40 years took part in each experiment. They gave informed consent and were free from any contraindications that prevent scanning. Demographic details are given in table 4.1

Table 4.1
Subject Demographics

SUBJECT NUMBER	GENDER	HANDEDNESS	AGE
1	M	R	39
2	M	R	40
3	M	R	23
4	M	R	28
5	M	R	35
6	M	L	32
7	M	R	37

All experiments were performed using an ABA design with 5 repeats of 30 second presentations of target (A) and reference phases (B). The total scan time for each experiment was 5 minutes. In each subject, the colour perception experiment preceded the colour imagery experiment.

4.4.2 Experimental design and procedure

Stimuli for colour perception

Stimuli were projected onto a screen placed across the bore of the MR magnet 1.8 metres from the subjects' eyes. The target phase consisted of a Mondrian pattern composed of eight differently coloured swatches (figure 4.1). The Mondrian alternated at 1 Hz with a featureless screen of the same mean luminance and hue. In the reference phase, the colours were replaced by differing levels of grey and the resulting achromatic Mondrian alternated at 1 Hz with a screen of the same mean luminance.

Table 4.2
Summary of paradigm for the perception of colour

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Colour Mondrian alternating at 1Hz with a featureless screen of same mean luminance	Watch display
OFF	Achromatic Mondrian alternating at 1Hz with a featureless screen of same mean luminance	Watch display

Stimuli for colour imagery

A series of pre-recorded questions (Howard, 1997 personal communication, see appendix A1) was presented at a rate of 1 every 10 seconds via pneumatically driven headphones. In the target phase, the questions all involved the relative darkness of the colour of commonly encountered objects, for example; 'is a canary darker yellow than a banana?' or, 'is a strawberry darker red than a raspberry?". Subjects indicated a Yes/No response by pressing one of two buttons. The questions were chosen to have high imageability and subjects were instructed to use the questions as cues to image the relevant colour until they heard the next question, and to use imagery to answer the questions. In the reference phase, a version of the clockface task (Corballis & Sergent, 1988) was administered. Subjects were presented with a series of times, 'twenty to seven' or 'a quarter past six", for example, and were asked whether the angle between the minute and hour hands of a clock would be greater or less than 90 degrees.

Table 4.3
Summary of paradigm for the colour imagery

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Questions of hue discrimination Example "is a strawberry darker that a raspberry"	Image the relative colours of the object in the "minds eye" and respond yes or no via a button press
OFF	The "clock task" question of times . Example twenty to seven	Image the time on an analogue clock and respond via a button press if the hand of the clock are greater or less than 90^{o}

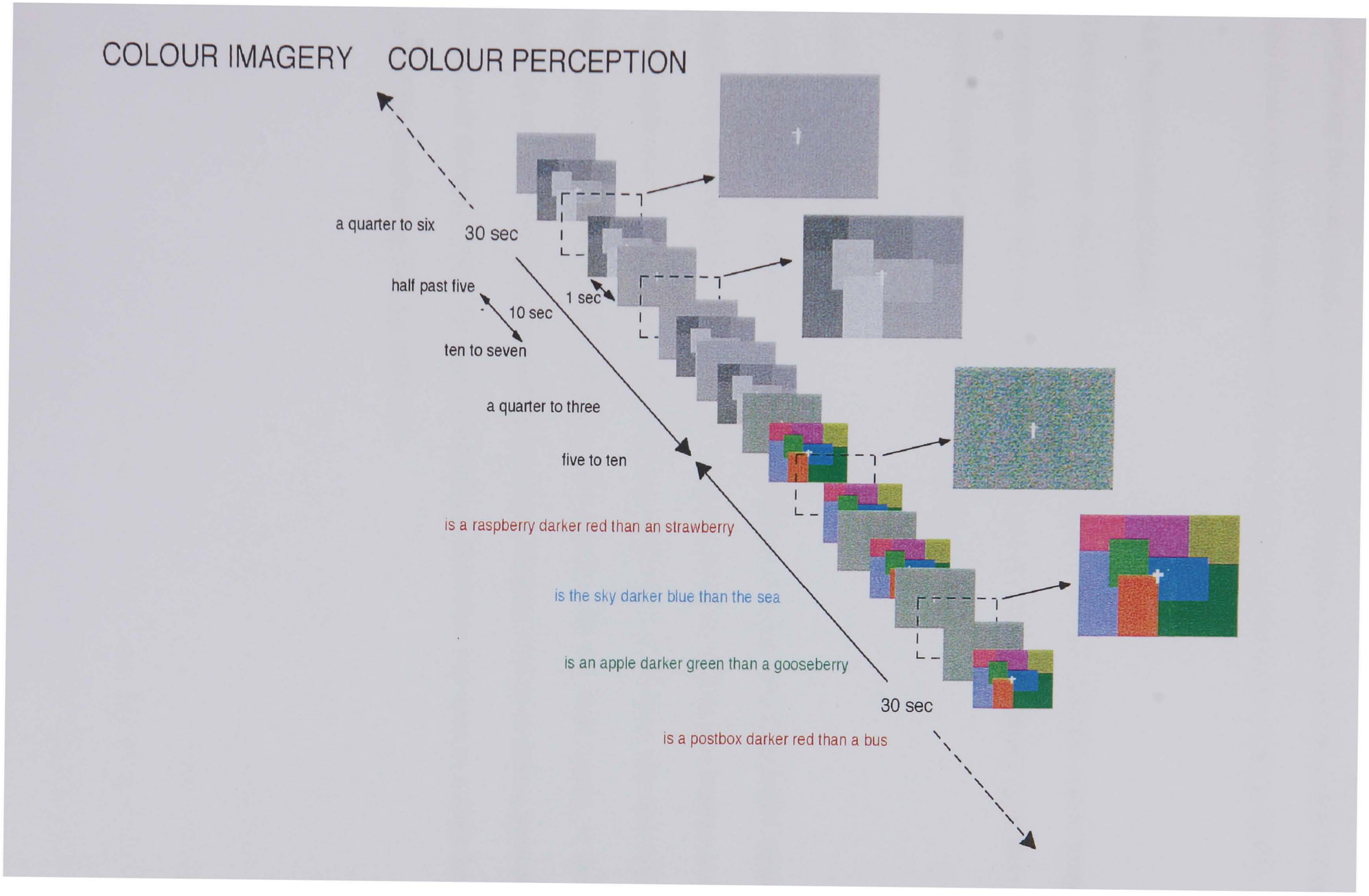


Figure 4.1: Stimuli used in the perception and imagery of colour experiments

4.5 Behavioural Results

The responses and response times were recorded on-line as the subjects were performing the tasks inside the scanner. Mean reaction times for the colour imagery and clock tasks were equivalent (757 ms *vs* 676 ms, respectively; t=1.83, $p > 0.05$).

4.6 Neuroimaging Results

During post-scan debriefing, all subjects reported vivid and sustained colour imagery experiences while carrying out the task. The generic brain activations ($p<0.001$) for colour imagery and perception are presented in figure 4.2.

4.6.1 Perception of colour

Colour perception activated a distributed network of areas which included bilateral regions in the posterior fusiform gyms, a region identified in previous studies as area V4 (Lueck et al., 1989; Zeki et al., 1991) (see table 4.4). Activation was also seen in the right anterior lingual gyuss, striate cortex and the left and right insula. A similar network of areas has been described in previous imaging studies of colour perception (Gulyas & Roland, 1994). An area of anti-phase activation was seen in a more lateral part of the fusiform gyrus (see table 4.5)

Table 4.4
Major regional foci of activation for colour perception

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Colour Area V4	-35	-64	-13	20
	-12	-78	-13	18
Insula	-38	3	-7	9
Midline				
Primary Visual Area	0	-81	4	45
Right Hemisphere Regions				
Colour Area V4	26	-78	-13	11
Fusiform gyrus	12	-50	-2	30
Insula	38	14	4	5

Table 4.5
Major regional foci of anti-phase activation for colour perception

AREA	X	Y	Z	CLUSTER SIZE
Right Hemisphere Regions				
Fusiform gyrus	29	-58	-7	16

4.6.2 Imagery of colour

Colour imagery activated a different but closely related network of areas to colour perception, with activity in the right anterior fusiform and parahippocampal gyri and hippocampus as well as the left insula (see table 4.6). No activity was observed in the region identified as area V4. This result interestingly does not support an fMRI study which reported activation of the posterior fusiform gyrus when experiencing simple coloured afterimages (Sakai et al., 1995).

Similar areas within the right middle fusiform gyms were activated during the non-colour reference phase of both perception and imagery paradigms. Since the cognitive operations engaged by the clockface task and viewing the achromatic Mondrian are so different, it is likely that these sites of anti-phase activation seen in the right middle fusiform gyms represent suppression of activity during perceptual or imaginal processes involving colour (see table 4.7)

Table 4.6
Major regional foci of activation for colour imagery

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Insula	-38	8	-7	8
	-43	19	-2	7
	-40	0	9	2
Right Hemisphere Regions				
Fusiform gyrus	40	-56	-13	6
Hippocampus	26	-42	-7	4

Table 4.7
Major regional foci of anti-phase activation for colour imagery

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Lingual gyrus	-9	-47	-2	8
Hippocampus	-14	-22	-2	8
Right Hemisphere Regions				
Fusiform gyrus	40	-56	-7	9
Hippocampus	9	-36	-2	7

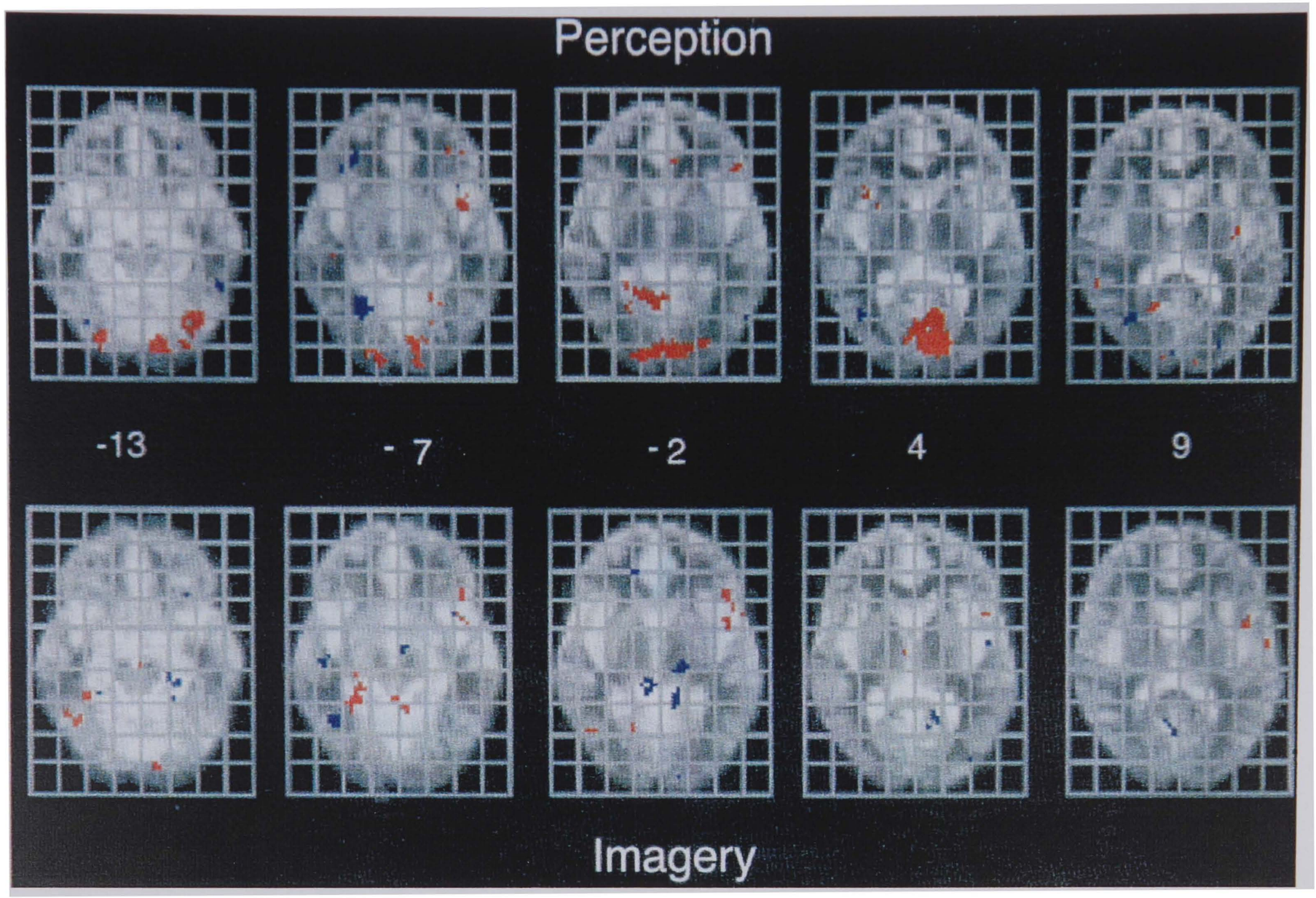


Fig. 4.2. Generic brain activation maps coregistered onto a template brain. Summary images from generic brain activation maps showing activations during colour perception and imagery experiments. Voxels coloured red are those indicating activation during target (colour) phase of perception end imagery paradigms. Blue voxels indicate apparent activation during reference phase or deactivation during target phase.

4.7 Discussion

Direct comparison of imaginal and perceptual networks was made possible by scanning each individual for both experiments in a single session during which the subjects' position in the scanner remained constant. The target phase of the colour imagery task required the subjects to make a hue judgement from memory: which of two similarly coloured objects was the darker. Colour imagery was therefore essential to perform the judgement involved in this condition. This was contrasted with the reference condition; judging whether the hands of a clock face formed an angle greater than 90 degrees at a given time. Although these task may not seem perfectly matched in terms of the "cognitive insertion" principle discussed in chapter 2 earlier. Both tasks entailed image generation, inspection and an "either/or" judgement with only the target phase making reference to colour (Figure 4.1).

As detailed in section 4.1.2 patients with impaired visual percepts often have parallel deficits of visual imagery (DeRenzi & Spinnler, 1967; Symonds & Mackenzie, 1975; Goldenberg et al., 1987). This supports the notion that imagery and perception share common neural substrates. However, these functions cannot share completely identical processing networks. The most straightforward reason for making a distinction is that such deficits have also been found to be dissociable (Beauvois & Saillant, 1985; Chatterjee & Southwood, 1985).

The neurological site for object-colour storage is of considerable interest to models of knowledge storage. If anatomical distinctions can be found between areas associated with the imagery for object colour and those for other stored knowledge, it adds support to the functional dissociations reported.

Such evidence has recently become available. It is clear that with respect to colour perception, there is no precise overlap in neural networks with those used for object-colour imagery as claimed by Farah (1988). The retrieval of object colour must be based on relatively distinct neural networks, since impaired imagery for object colour can accompany preserved imagery for object shape (Stengel, 1948). Moreover, a patient with acquired achromatopsia, following bilateral destruction of lingual and fusiform gyri, was able to perform a colour hue discrimination task similar to that used in the current study (Shuren et al., 1996). Together with a further case (Case 2, De Vreese, 1991), whose colour perception was intact but who could not derive colour information from recalled images, such patients illustrate an apparent "double dissociation" between deficits in perception and imagery.

Consistent with this, a recent study published after this experiment was conducted, suggested that retrieval of information about the specific object attribute of colour does not require reactivation of brain areas that mediate the perception of that colour (Chao & Martin, 1999). During separate PET scans, subjects passively viewed coloured and equiluminant gray-scale Mondrians, named coloured and achromatic objects, named the colour of coloured objects, and generated colour names associated with achromatic objects. Colour perception was associated with activations in the lingual and fusiform gyri of the occipital lobes, consistent with previous studies. Retrieving information about object colour (generating colour names for achromatic objects relative to naming achromatic objects) activated the left inferior temporal, left frontal, and left posterior parietal area (Martin et al., 1996)

When subjects retrieved colour names for achromatic objects relative to the baseline of viewing grey-scale Mondrians, additional activations were seen in the left fusiform gyri. However, these areas were lateral to the occipital regions associated with perception and were identical to occipital regions activated if subjects simply named achromatic objects relative to the same baseline. The authors suggest that the occipital activation associated with retrieving colour information was due to perception of object form rather than to the top-down influence of brain areas that mediate colour perception.

This fMRI study likewise demonstrates the anatomical separation of colour imagery and perception regions that once again explains this apparent dissociation between imagery and perception. Lesions of the fusiform gyrus that spare more anterior areas (Shuren et al., 1996) may lead to deficits of perception but not imagery, while lesions affecting anterior areas, but sparing more posterior ones (Case 2 (De Vreese, 1991), may result in normal colour vision with impaired colour imagery. It therefore follows that those more extensive lesions affecting both anterior and posterior areas would result in deficits in imagery and perception (Riddoch & Humphreys, 1987).

The colour imagery task used in this study also involved the imagery of objects with their associated colour and compared this with the imaged colour of another object. This imagery task was designed so that it forced an imagery strategy to be adopted by the subjects. If we had relied on colour knowledge alone, e.g. "what colour is a banana?" the subject could have answered by semantic information alone and not engaged regions of the cortex involved in imagery

Interestingly, although colour seems to be encoded visually rather than verbally in episodic memory (Watkins & Schiano, 1982), inspection of a coloured object during imagery appears to occur without activation to early visual areas V1/V2. While some neuroimaging studies have shown activity in areas V1/V2 (Engel et al., 1997; Kleinschmidt et al., 1996; McKeefry & Zeki, 1997), in addition to extrastriate regions, when subjects view coloured stimuli (for location of these areas see figure 4.3), the results here instead support the view that visual imagery is associated with activity in occipito-temporal and occipito-parietal regions (Roland & Gulyas, 1994, 1995), and do not address the role played by V1. Although V1 was not activated equally by the target and reference phases of the colour perception stimulus, it is conceivable that this region was active in both the phases of the imagery experiment and thus no apparent V1 activation was seen (Kosslyn et al, 1995; Le Bihan et al., 1993). Finally, one further explanation as to why colour imagery should be independent of activity in area V4 might be that V4's role in normal vision is to achieve colour constancy across different lighting conditions (Zeki, 1983) a role that might be irrelevant in visual imagery.

The activity in a region of the fusiform gyrus anterior to V4 in man and close to the activation reported here for colour imagery has been reported in studies of colour knowledge (Martin et al., 1995), and implicated in a study of colour naming (Chao & Martin, 1999)

The precise anatomical localisation of the activation seen in colour perception and imagery is not simple, as there is little agreement between the colour centre in humans and monkeys. Recently, there have been claims that the colour centre in the human

that is homologous to the colour area in primates is located in area TEO rather than in V4 of the macaque cortex and as such has been given a new name V8 (Hadjikhani et al., 1998). Thus the relation of V4 in human to areas TEO (Boussaoud et al., 1991) and V8 described as anterior to V4 in the monkey is unclear. The presence of colour areas distinct from V4 may represent a hierarchical pathway located within the human temporal lobe along which colour information from early visual areas is made available to higher order systems responsible for colour knowledge and imagery. However, it is clearly a topic of ongoing debate (Zeki et al, 1998; Tootell & Hadjikhani, 1998; Heywood & Cowey, 1998).

4.8 Conclusion

The main aim of this study was to compare colour perception and colour imagery in humans and to investigate the possible areas of convergence. This was made possible by scanning subjects in the same scanning session on both tasks. This turned out to be vitally important with the current debate currently taking place with regard to the "name" and location of the colour centre (Tootell & Hanjikhani, 1998; Zeki et al., 1998). The inclusion of a control colour perception task to compare with colour imagery allowed us to directly map these cognitive processes on to the human brain rather than to comment on the functional equivalence of human and primate cortical areas (see figure 4.3).

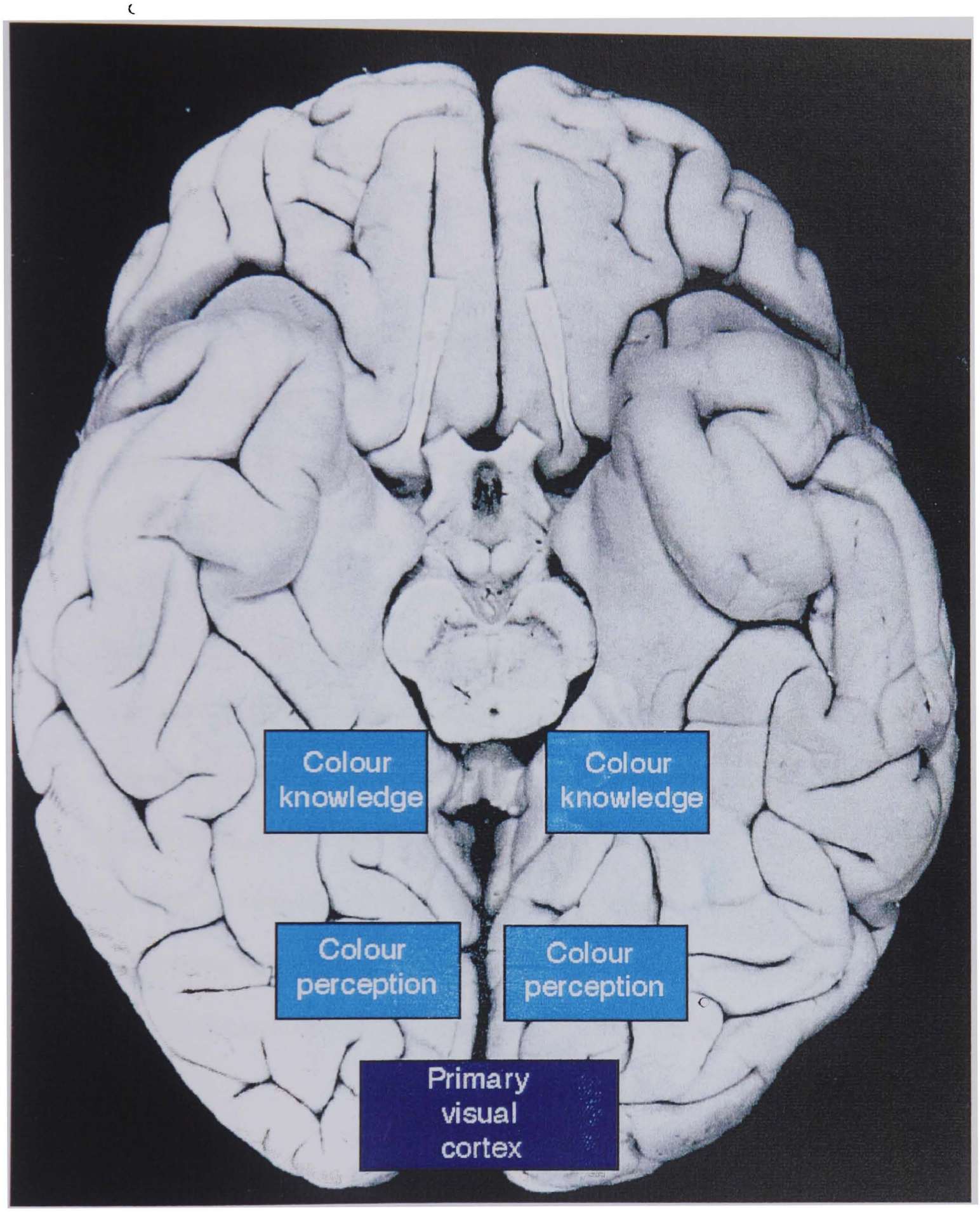


Figure 4.3: Relative anatomical locations for colour perception and colour imagery

Chapter 5: The Functional Anatomy of Illusory Colour

Barnes et al., (1999). The functional anatomy of the McCollough contingent colour after-effect. *NeuroReport* 10 (1) 194-198.

5.1 Introduction

The visual system readily adapts to a tremendous range of intensities. Neither the adaptation process itself nor its subsequent decay is instantaneous. Consequently, the visual system displays after-effects due to previous stimulation. For example, exposing the eyes to a light intense enough to bleach the visual pigment will result in the after-image that may last for up to 30 minutes. The after-effect from such intense stimulation is limited to the eye originally stimulated and is thought to be generated peripherally, at the eye, rather than centrally (Craik, 1940). The classic explanation for the occurrence of visual afterimages was formulated by Hecht, (1937) and assumes that the afterimages are entirely the consequence of bleaching and regeneration of the visual pigments. However, subsequent studies have shown that adaptation to light can occur without any measurable bleaching of the photo-pigments (Granit et al., 1938; Pirenne & Denton, 1952). Adaptation resulting from relatively low levels of stimulation is presently assumed not to occur within the retina but at a neural level rather than at a receptor level (see Skowbo et al., 1975) lasting after effect using moderate levels of illumination is the McCollough Effect (ME) (McCollough, 1965).

In the previous chapter, colour perception and imagery involved distinct but overlapping networks of cortical regions, which suggests a neurological vulnerability to hallucinations leading subjects, under certain conditions to combine and misinterpret internally and externally generated colours. In this chapter, two

experiments are reported which were specifically designed to discriminate the neural regions involved in the perception of colour from those involved in the perception of illusory colour seen in the McCollough Effect. Direct comparison of these different perceptual process may elucidate further on the mechanisms of hallucinations, as the colour seen in the McCollough effect is not an "external" percept but is an "internal" image, involuntarily projected into the outside world.

5.2 Studies of the McCollough Effect

The ME was first described in 1965 as an orientation specific colour after-effect. It is typically generated during an induction period as an observer is presented with two patterns of chromatic gratings that alternate every few seconds. The stimuli generally employed during induction are described as being "simple, repetitive, redundant and highly predictable patterns" (Dodwell & Humphrey, 1990). The chromatic grating patterns can be comprised of vertical black strips on a green background and black strips on a red background. Subsequently, when participants are presented with achromatic vertical and horizontal patterns, complementary colour after-effects appear that are contingent on orientation. That is, the achromatic background on the vertical grating appears pinkish and the achromatic background on the horizontal grating appears greenish. A 90 degree rotation of the test pattern causes the colour to exchange places, and a 45 degree rotation cancels the colour after-effect all together.

Since McCollough's original findings, many studies of this phenomenon have confirmed and extended her initial findings (see Skowbo et al, 1975). One issue that has occupied many vision researchers over the years since 1965 is what are the mechanisms that mediate the effect. Does the ME belong to early vision or to some

higher-level cortical stage? Many aspects of the effect suggest it is due to adaptation of mechanisms at an early stage of visual processing. It has been proposed that it is area 17 or V1 of the visual cortex that appears to have the necessary properties to mediate the ME (Skowbo et al, 1975)

McCollough originally proposed that the after-effect was the product of colour adaptation of edge detector mechanisms in the visual system; neurons found in V1 fit such a description. These detectors respond with decreased sensitivity to those wavelengths that have been adapted, or with which they have been more strongly stimulated. Edge detectors had been previously identified as coding for local orientation, however this was the first suggestion that these neurons could be involved in colour adaptation (McCollough, 1965). McCollough explained her effect as the "colour adaptation of oppositely orientated, vertical edge detector systems". She proposed that the after-effect was not due to ordinary negative afterimages, because it is linked to the orientation of the achromatic grids, whereas an afterimage is best viewed on a homogenous surface. Also, this after-effect appears even after equal exposure to complementary colours, and classical afterimages require either a fixation of the colour adapting stimulus or a very intense stimulus. The ME requires neither (Harris & Gibson, 1968).

Early research by Harris and Gibson (1968) confirmed that the ME was not a mere afterimage; however, it was suggested that the afterimage was more a product of "fatigued dipoles", a less complex unit than an edge detector. Mackay and Mackay (1973) offered another explanation of the ME. They proposed that the after-effect is due to changes at synaptic or subsynaptic levels through an "association network" of

units, which could identify the site of adaptation to a retinal level. In a later study, Mackay and Mackay (1975) suggested that simple fatigue of colour and orientation specific units is inadequate to account for the McCollough, and that an "associative habituation of synaptic coupling" might be at work.

Although certain parameters have been identified in the establishment of the ME, how and why the effect occurs is still open to debate. As mentioned, some of the earlier studies proposed that the effect was merely an afterimage, due to the adaptation of particular cells in the visual system. However, other researchers have proposed the process occurs at a level beyond the photoreceptors.

The neural adaptation model proposes that some stimulus is required to evoke the afterimage (Murch, 1979). It was suggested that the chromatic adaptation of postneural units is sensitive to a specific feature and colour. The colour after-effect can only occur if the units processing the test pattern are the same ones that were adapted during inspection.

The effect itself, having been identified as not being a simple afterimage, nor being the result of the adaptation of edge detecting mechanisms alone, may be due to a "two stage process" proposed by Riggs et al., (1974). They suggested that a sequential order is followed in analysing the after-effect, with the first stage being colour sensitive and the second stage being orientation sensitive, as mediated by central, rather than peripheral neural unit.

The after-effect generated in the ME has usually been found to be limited to the eye stimulated during training. In fact, several studies have reported that the ME does not transfer to the untrained eye even if it is made contingent upon a spatial after-effect that does transfer (Murch, 1972; Stromeyer, 1972). However, two studies have reported a weak, complimentary effect in the untrained eye (Mikaelian,1975). Mackay and Mackay (1973) reported the first instances of binocular interaction in the ME. In these studies, alternating achromatic vertical and horizontal gratings presented to one eye were paired with alternating red and green fields presented to the other eye. Subsequently, when only achromatic stimuli were presented, subjects reported negative orientation-specific after-effects in the eye which originally saw colours (the ME) but positive after-effects in the eye which was originally shown achromatic gratings.

White and Riggs (1974) presented a series of experiments investigating the use of angled stimuli in the production of the ME. While there was no evidence of binocular transfer, if the effect was limited to one eye during training, a binocular interaction effect was reported. Specifically, subjects were presented gratings of parallel lines to each eye which formed an angle as a result of binocular fusion. The direction, either up or down, of this fused angle was alternated, and each orientation was paired with a colour. Subjects subsequently reported MEs specific to the orientation of the angles, thus showing that a binocular interaction had occurred. The authors concluded that the resultant after-effect must not be due to narrowly tuned mechanisms (such as channels for spatial frequency or line orientation), but can be explained by a "neural substrate with characteristics like those reported for higher-order hypercomplex cells in the visual cortex".

Binocularly selective cells respond either exclusively or at least preferentially, when stimuli are presented simultaneously to both eyes. Vidyasager (1976) reasoned that binocular transfer of the ME had not been reported because binocularly selective cells were not optimally stimulated in these studies. Consequently, Vidyasager designed his study in such a manner that any orientation-specific colour adaptation at a binocular site could be recognised. A ME was obtained by presenting pairs of colour and line grid stimuli simultaneously to both eyes. In addition, complimentary pairings of line orientation and colour were presented to each eye, the hypothesis being, that any monocular effects would be cancelled out, leaving only a binocularly specific ME. The results, in general, agreed with the prediction, and therefore supported White and Riggs view that binocular, and thus presumably central effects do occur in the ME.

In the White and Riggs (1974) study, subjects fused two grid patterns to form an angle, which was simultaneously associated with a colour. It is of course, theoretically possible to do the reverse experiment: have subjects fuse two colours while being simultaneously shown a line orientation. No experiment employing a fused colour as the basis of ME has been published, though a number of studies examining dichoptic colour mixing have been reported (DeWeert & Levelt, 1976).

Hecht (1928) viewed the binocular fusion of red and green to form yellow as evidence of a central process in the formation of both monocular and binocular yellow. It is now thought that monocular yellow is formed at a peripheral site, probably at or before the level of the retinal ganglion cells (DeValois, 1967). The physiological location of the synthesis of the dichoptic yellow from the monocular red and green is less certain. De Weert and Levelt (1976) have postulated that dichoptic yellow results

from the "spill over" stimulation of yellow-blue channels in each eye as a result of the red or green input. They do not explain the mechanism by which red and green channels are cancelled leaving only yellow. Nevertheless, it is clear from their discussion that they reject the possibility of a centrally formed yellow and instead support a peripheral synthesis

These studies provide inconclusive evidence for the "adaptation" model of the ME, with the exact mechanism involved yet to be identified. Unless more conclusive evidence for the mechanism involved can be provided, or if the image is not the result of the adaptation of neural units or edge detectors, then a different approach is required in order to explain the effect.

In recent years, a number of parallels have been noted between the ME and classical conditioning, with the strongest evidence coming from the data on "decay" of orientation-specific after-effects. A number of the features of the "fade-out " process appear to be more similar to extinction phenomena from learning than to the decay of high intensity after-effects (Skowbo et al., 1974). First, the ME has often been found to persist for several hours, too long for adaptation to be the entire mechanism. Second, while an adaptation process would be expected to decay in darkness, the ME "fades-out" most rapidly in the presence of an achromatic stimulus with the same pattern of lines as was used during acquisition (Murch, 1976).

Some researchers (Teft & Clark, 1968; Stromeyer, 1972) have examined the specificity of the ME for the orientation of lines used during acquisition. In general, the ME becomes weaker as the discrepancy between the line orientation of the

acquisition and the test stimuli is increased. This result is analogous to examples of stimulus generalisation found in many learning studies where the frequency or strength of a response decreases as the difference between learning and test stimuli is made greater. Furthermore, Murch (1976) reported results that were interpreted as evidence of the spontaneous recovery of orientation-specific afterimages

Recently there has been much speculation on the possible underlying neural systems. Proposed physiological sites include the retina, the lateral geniculate nucleus, and the early visual cortex (e.g Harris & Gibson, 1968; Stromeyer & Dawson, 1978). The interaction of two or more neurons has also been proposed to account for the various aspects of ME (e.g. Savoy, 1984). Evidence from patients with brain lesions has provided some evidence on the site of the ME. Patients with known deficits in memory have been found to have MEs of a strength and duration comparable to normal control subjects. Savoy and Gabrieli, (1991) studied the ME in 11 subjects, 5 subjects with various severity of Alzheimer's disease (AD), patient H.M., who has had global amnesia due to bilateral medial temporal lobectomy (Milner, 1968), and 5 control subjects. They found normal MEs in all subjects and concluded that there is a dissociation between the ME and the learning mechanisms that mediate recall and recognition. They went on to say that from what is known about the neuropathology in H.M and AD the findings were consistent with other evidence implicating early visual areas, especially V1, as a plausible site of the ME. Studies have suggested that the ME is as a result of the adaptation of striate neurons that code simultaneously for orientation and colour (Michael, 1978). It has also been suggested that the site of the colour component of this effect could be the colour-sensitive cells found in the "blobs" of area V1 (Livinstone & Hubel, 1984). These colour sensitive cells found in

the "blobs" may interact with other cells in area V1 that are both sensitive to orientation and spatial frequency, and it is a change in connection strengths between these cells that give rise to MEs (Savoy, 1984).

Patients with visual form agnosia as a result of carbon-monoxide poisoning (Humphrey et al., 1991) and cortical blindness (Humphrey et al., 1995) have also been found to have a normal ME. Humphrey et al., (1991) studied a patient D.F., who had developed an extreme visual agnosia following exposure to carbon monoxide. Magnetic resonance imaging revealed damage to area 18 and 19, although V1, area 17 remained largely intact. The patient had great problems in recognising the simplest of geometric forms and had difficulties discriminating the orientation of objects (Goodale, et al., 1991; Milner, et al., 1991). However, it was possible to investigate her susceptibility to the ME as her colour perception was found to be normal (Milner, et al., 1991). The result of this study showed that D.F had normal ME and indeed reported after her second session of adaptation that the after-effect was present some 20 hours later. Given the result of the brain scan and her ability to be see the appropriate colour after-effect in the ME the authors argue that the results are consistent with area V1 having the necessary properties for the site of the ME. Recently, a second study by the same group (Humphrey, et al., 1995) concluded again that it was likely that the mechanisms underlying the ME were situated in the primary visual cortex or maybe earlier in the visual pathway. This study examined a patient, P.B, a 39 year old male who had extensive brain damage as a result of trauma. He was essentially "cortical" blind and unable to process form for perceptual discrimination or visuomotor control. However, like D.F he had intact colour perception and showed the normal ME.

To help localise the cortical visual structures that may be directly involved in the perception of illusory colour, a functional magnetic resonance imaging (fMRI) study of the McCollough effect was recently performed by (James et al., 1998). To examine the relationship between the McCollough effect and cortical activity the group used high-resolution fMRI after McCollugh adaptation. In various conditions, subjects were presented with "congruent" and "incongruent" test patterns that had the same orientations as the inducing stimuli and thus would evoke the McCollough effect, and with "noncongruent" test pattens that were 45 degrees from the inducing stimuli and would not evoke the effect.

From what little information is available about the study, from the published abstract, yhey observed activation in areas VI/V2, and in the fusiform and lingual areas, which they claim to be in agreement with earlier research on colour afterimages (Sakai et al., 1995). However, the group did not carry out a control experiment of viewing a coloured display with which to validate their results, neither did they scan the whole brain thus potentially losing vital information on the cortical network involved.

5.3 Rationale and Aims

The present study reports on two experiments which examined the neural substrate of the ME utilising functional magnetic imaging (fMRI). The first experiment contrasted viewing of monochromatic test patterns, one of which was constructed to later show the ME, while the second experiment contrasted viewing coloured test pattern against the monochromatic counterpart.

The experiments therefore, were able to examine activation mediated by neural systems in both viewing a coloured pattern and when experiencing the ME. We predicted that regions activated in the ME experiment would include fusiform and lingual areas, as well as additional cortical areas specific to any cognitive components involved in the phenomenon. Such additional activation would have strong implications for a plausible neural mechanism for the ME.

5.4 Methods

5.4.1 Subjects

Six subjects volunteered to take part in the study. Their mean age was 32, ranging from 23 to 39 years. All subjects reported having good eyesight and gave their informed consent and were free from any contraindication to scanning.

Table 5.1
Subject demographics

SUBJECT NUMBER	GENDER	HANDEDNESS	AGE
1	M	R	23
2	M	R	39
3	F	R	29
4	F	R	36
5	M	R	31
6	F	R	35

Prior to scanning the subjects were made fully aware of the instructions and acknowledged that they understood their task while in the scanner.

5.4.2 Induction Phase.

Prior to scanning, each subject underwent an induction phase which consisted of viewing test patterns with a spatial frequency of 1.5 cycles per degree displayed on a computer monitor which were designed to induce the ME. The subjects viewed two test patterns alternately for a 9 second period with a one second gap between patterns. This gap comprised a black white screen. The total induction was for a period of 30 minutes. The test patterns were circular in outline and consisted of a red and black horizontal grating and a green and black horizontal grating (see figure 5.2). All subjects reported they were experiencing the ME after the induction period. Subject adapting patterns were viewed binocularly and no head restraint was used.

5.4.3 Experimental phase

During the experiment, the stimuli were projected by a computer controlled projector system onto a screen placed at a distance of 1.5 metres from the subjects' eyes and viewed by subjects through a prismatic mirror. The target phase was viewed first by the subjects in each of the experiments.

Stimuli for colour perception

In the ON phase subjects were showed separate test patterns of vertical red and black horizontal gratings for 4 secs then by a one second blank white screen followed by green and black horizontal gratings. The OFF phase involved viewing a series of achromatic grids at 45° for 4 secs separated by a blank screen. A summary of the stimuli is given in table 5.2. As in the adaption phase each grating was circular in outline and had the same spatial frequency.

Table 5.2
Summary of paradigm for the perception of colour

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Red/black vertical grating & blue/black horizontal gratings with a spatial frequency of 1.5 cycles per degree	Watch coloured grating
OFF	Achromatic gratings at 45° with a spatial frequency of 1.5 cycles per degree	Watch achromatic gratings

Stimuli for McCollough Effect

In the ON phase subjects viewed alternating horizontal and vertical achromatic grids (intended to elicit the illusion of colour) for a period of 4 secs separated by a blank screen. The OFF phase consisted of viewing achromatic grids at 45° as in the colour perception experiment. See summary table 5.3.

Table 5.3
Summary of paradigm for the McCollough effect

CONDITION	STIMULI	TASK INSTRUCTIONS
ON	Horizontal and vertical achromatic gratings with a spatial frequency of 1.5 cycles per degree	Watch achromatic gratings
OFF	Achromatic gratings at 45° with a spatial frequency of 1.5 cycles per degree	Watch achromatic gratings

Experiment 1: Colour Perception

Target Phase A

Reference Phase B

Experiment 2: McCollough Effect

Target Phase A

Reference Phase B

Figure 5.1 Stimulus used for colour perception and the McCollough effect

5.5 Results

Generic brain activation maps are shown in figure 5.1. The false positive activation ratio was set such that 30 random type one errors would be expected in the area of the brain examined. The threshold was set by randomisation (Brammer et al., 1997). This corresponded to voxels with a probability of false positive activation < 0.0015

Colour perception

The coloured patterns in Exp.1 produced a small but significant increase in signal intensity in the fusiform gyrus (BA19), the insula and primary visual cortex only (see table 5.4.).

Table 5.4
Regional activations in colour perception.

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Fusiform Gyrus (V4)	-29	-58	-13	4
Primary Visual Cortex V1/V2	-6	-92	4	5
Insula	-32	-19	-2	2
Right Hemisphere Regions				
Fusiform Gyrus	23	-52	-7	2

The co-ordinates suggest the location to be area V4, as determined previous work (McKeefry & Zeki 1997). Studies using multi-coloured "Mondrian" stimuli show that the location of V4 in the left hemisphere can vary between individuals by as much as 34mm in the anteroposterior (y) axis and 24 mm in the dorsoventral (z) axis and even after averaging across subjects, variations in location of 10.7mm in the y axis and 3.95mm in the z axis are evident (McKeefry & Zeki 1997). The pattern seen

here including the left insula activation is consistent with previous colour perception neuroimaging studies (Howard et al., 1998).

Ilusory colour perception

All subjects reported seeing colours when viewing achromatic vertical and horizontal lines (the ME). The illusory colour activated the left anterior fusiform gyrus, but significantly, no activation was seen in the primary visual cortex (V1). Of particular note is the robust activation outside the temporo-occipital cortex including the right and left ventrolateral prefrontal cortex (see table 5.5)

Table 5.5
Regional activations in the McCollough effect

AREA	X	Y	Z	CLUSTER SIZE
Left Hemisphere Regions				
Fusiform Gyrus	-40	-53	-7	6
Ventrolateral Prefrontal Cortex	-40	36	-2	33
Insula	-49	11	4	6
Right Hemisphere Regions				
Fusiform Gyrus	35	-47	-13	6
Ventrolateral Prefrontal Cortex	46	22	-2	20

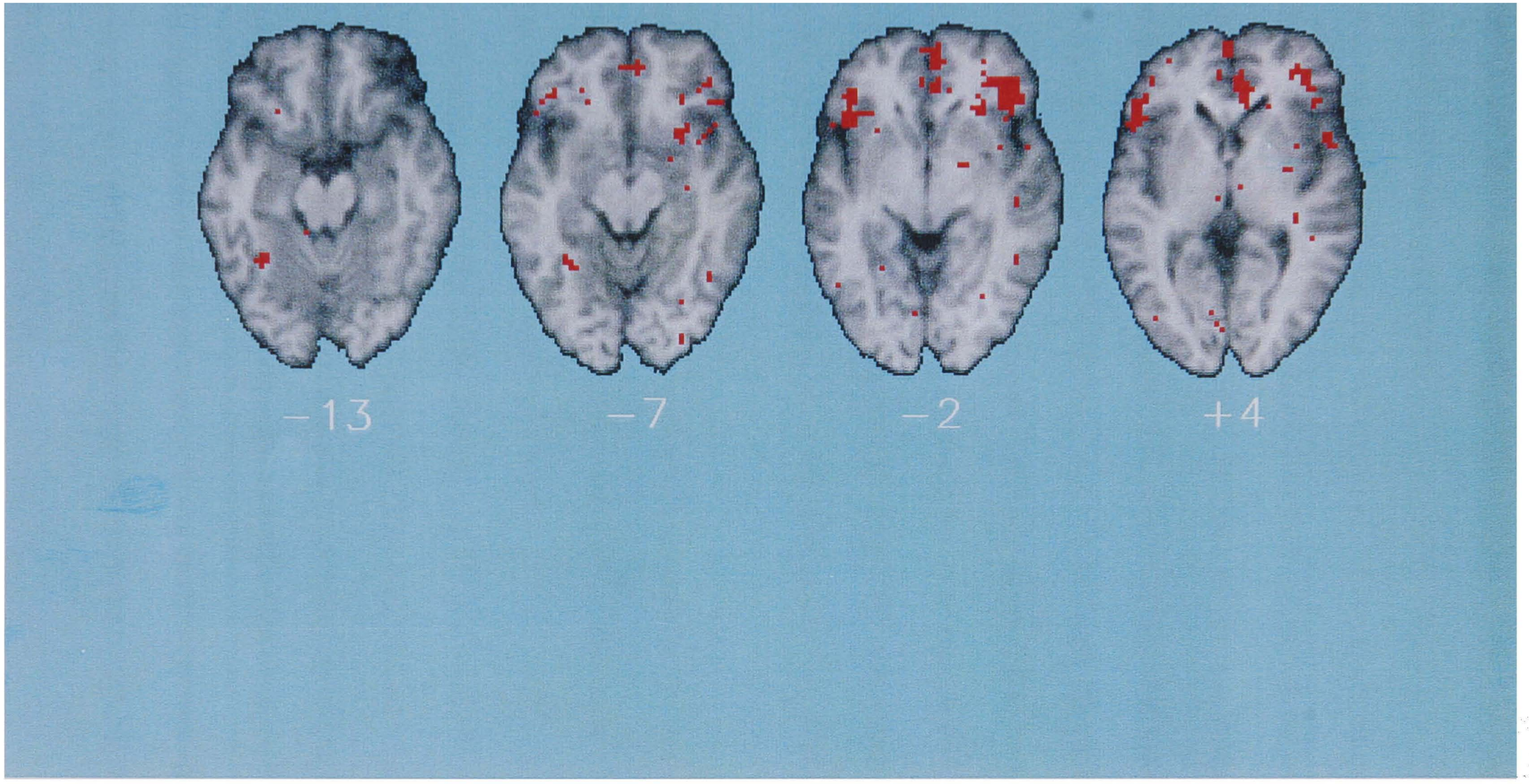


Figure 5.2. A Generic Brain Activation Map (GBAM) of the McCollough Effect showing activations during experiment 2. Activated clusters (in red) were in the fusiform gyri (right: 35 -47 -13; left -40 -53 -7), ventrolateral prefrontal cortex (right: 43 25 -2; left: -40 36 -2) and left insula (-49 11 4).

5.6 Discussion

In this study we have mapped the cortical activation of subjects when viewing illusory colour as in the McCollough contingent after-effect. This was made possible by scanning each individual performing the McCollough task and an equivalent colour perception task in the same session. Perception of the visual attribute of colour in the perception condition (Exp. 1), was associated with activity in an area described in previous studies as being V4 (McKeefry & Zeki, 1997). An illusion of the same attribute produced a different pattern of activation and, most strikingly, there was lack of activity in the area of V4. The viewing of the McCollough stimuli instead activated the left anterior fusiform gyrus, an area previously identified as having a role in the colour naming (Martin et al., 1995). It should be noted that the ME is not a simple retinal after-effect, which have been studied using fMRI and which also appears to activate the fusiform gyrus (Sakai et al., 1995: Hadjikhani et al., 1998)

Activation of the primary visual areas (V1/V2) was evident in exp. 1 when subjects viewed the red/black, green/black grids. Activation in this area has been noted in previous imaging studies of colour (McKeefry & Zeki, 1997). Interestingly, this V1/V2 activation was absent in the illusory condition. This could be as a result of V1/V2 being equally activated in both the target and reference phases or that the colour seen in the ME is due to a different mechanism involving higher cognitive aspects. A further explanation as to why illusory colour does not activate V1/V2 might be that the cells in this area seem to be important in wavelength discrimination (Kulikowski et al., 1994) a role that might be irrelevant in the perception of illusory colour.

We did not predict extensive frontal activation specifically in the ventrolateral prefrontal cortex when viewing illusory colour, which we assume, reflects additional processing underlying the ME. Activity in such areas has been associated with visual working memory (Courtney et al., 1998), and when comparing normally coloured objects with their black and white counterparts (Zeki & Marini, 1998). This pre-frontal activation cannot be attributed to "bottom up" effects such as the fatiguing of neurons in the early visual areas. This prompts us to speculate that the process that produces the colour illusion is a process related to a "top-down" mechanism. These findings are relevant to the issue of a "colour processing stream" (McKeefry & Zeki, 1997) that may be hierarchical in nature, where the fusiform gyrus has a essential role, and additional areas of activation such as frontal and temporal cortex may represent higher levels of processing of colour and that a "top-down" processing mechanism is implicated in this colour contingent after-effect.

5.7 Conclusion

In this study we have mapped the activation associated with the McCollough illusion. We have demonstrated that the viewing of this illusion is associated with activity within the anterior fusiform gyrus, close to the area V4, previously reported as functionally specialised for the early processing of colour. Due to the close proximity of these brain regions which seem to have a role in colour perception, colour imagery and now illusory colour, the observation that hallucinating subjects confuse "actual" and "imagined" colours (see chapter 6) may be due to abnormal connectivity, physiological or psychological, between these brain regions.

SECTION 3: VISUAL HALLUCINATIONS

Chapter 6: Properties of visual hallucinations associated with Parkinson's disease

6.1 Introduction

According to the DSM IV criteria (American Psychiatric Association, 1994), an hallucination is "a sensory perception without external stimulation of the relevant sensory organ" distinguishing them from illusions, which are experiences in which an external stimulus is perceived but then misinterpreted. Although separate, the phenomena often overlap with illusions leading to hallucinations or hallucinations leading to illusions. This chapter examines visual hallucinations, first reviewing the incidence of visual hallucinations in the various psychiatric and other neurological diseases and then by a closer investigation of the psychological processes underlying visual hallucinations in patients with Parkinson's disease (PD).

The most direct categorisation and the one that is most pertinent to this review divides visual hallucinations into simple and complex hallucinations. Simple hallucinations are characterised by the absence of form, and are often simple photopsias such as flashes of light or colour. Occasionally, geometric shapes are described which move around in space. Simple hallucinations are often associated with a visual field defect and despite the complexity of the visual phenomena sometimes experienced, pathological involvement of the occipital lobes in not essential for their production (Weinberger & Grant, 1940). Complex visual hallucinations are characterised by visions that are clearly defined, have specific form and can include animals, objects and humans. They are experienced during full consciousness and are often described as possessing the attributes of size, shape, colour and motion of their real world

counterpart. Complex hallucinations are thought to involve the temporal cortex. A view supported by the complex visual hallucinations that can result from the experimental stimulation of the temporal region (Penfield & Perot, 1963), and which are experienced by patients with temporal lobe epilepsy (Kim et al, 1993).

One of the most common psychiatric disorders associated with hallucinations is schizophrenia. These hallucinations are often auditory but visual hallucinations have been reported to occur in up to 40% of patients (Mueser et al., 1990; Phillipson & Harris, 1985; Bacha et al., 1989) and are present more often in late paraphrenia (Howard & Levy, 1994). These visual hallucinations are usually formed complex images and consist of animals, people and events (Asaad & Shapiro, 1986). They generally appear suddenly and spontaneously, and do not change whether the patients' eyes are open or closed. In contrast, drug-induced visual hallucinations are simple with vivid colours and abstract images such as those associated with lesions to the occipital lobe (Asaad & Shapiro, 1986). They are usually preceded by uniform visual sensations, such as colour and shape and can be followed by formed images that are more readily seen with the eyes closed or in a darkened room. Visual hallucinations are also quite common in temporal lobe epilepsy, particularly with a left temporal lobe focus (Trimble, 1992) either during the aura or the ictal period itself (Slade, 1976). The type of hallucination experienced depends on when it occurs relative to the ictus. For example the type of image associated with the ictus is usually formed and complex, while those associated with the aura are simple.

Complex hallucinations can also be associated with tumours of the temporal lobe, the most common of which is glioblastoma multiforme (Horrax, 1923). In most instances

the tumour involves the primary visual pathway (the optic radiations) and produces a subsequent homonymous hemiaopia or quadrantanopia (Horrax, 1923). Visual hallucinations may also be associated with vascular lesions such as a stroke to subcortical or midbrain regions (Gellar & Bellur, 1987; McKee et al., 1990). It is usually an infarction in the posterior cerebral artery area, damaging the reticular activating system. These hallucinatory phenomena, referred to as penducular hallucinosis, are usually seen as bright vivid images that are sudden in onset with preserved insight (Starkstein et al., 1992). L'Hermitte described the first case (L'Hermitte, 1922), and associated the hallucinotic state with the dream state comparing the similarities of incoherence, visuotactile associations, abundance of mobile and coloured images, and the tendency for their nocturnal occurrences. He further proposed that hallucinations are the result of a "release phenomenon" secondary to damage to the reticular activating brainstem pathways. However, there is now evidence that some patients with penduncular hallucinosis have lesions in other brain areas including the midbrain, substantia nigra, subthalamus, basal ganglia thalamus and limbic regions (Feinberg & Rapcsack, 1989; Lanska et al., 1987), suggesting that penducular lesions are not necessary or sufficient to produce hallucinosis. Hallucinations can occur as a result of a temporo-parieto-occipital lesions (Starkstein et al., 1992). Memory disturbances and paranoid delusions also accompany lesions in this area, and typically involve seizures and subcortical atrophy as precursors (Starkstein et al., 1992).

Visual hallucinations can be found in elderly subjects with delirium, dementia, eye pathology, or a combination of these (Berrios & Brook, 1984; Weinberger & Grant, 1940; White, 1980). Such hallucinations are reported to be formed and brightly

coloured. Those associated with eye pathology or delirium last until blindness ensues or until the delirium resolves. Those found to occur with dementia have been linked with a 80-85% decrease in levels of choline acetyltransferase (ChAt) in the temporal and parietal cortices (Perry et al., 1990) and tend to become more prevalent as the degree of dementia increases (Perry et al., 1985).

Visual hallucinations are also common in late-onset neurological conditions especially Parkinson's disease (PD). There have been several recent surveys which give prevalence estimates of visual hallucinations between 9.8% and 44% (Haeske-Dewick, 1995; Sanchez-Ramos et al, 1996; Graham et al, 1997; Aarsland et al., 1999). The visual phenomena range from bizarre, complex and frightening "visions" to distortions of real percepts (illusions) such as a hat-stand appearing to turn into a person. Several risk factors have been identified for visual hallucinations: some authors state that dopaminergic drugs play a necessary part in the aetiology but comparisons of hallucinators and non-hallucinators have seldom shown major differences in drug history (see e.g. Sanchez-Ramos et al, 1996). It appears that the combination of dopaminergic drugs and cognitive impairment plus, according to some studies, psychiatric disorder is most likely to give rise to visual hallucinations. Although visual hallucinations can be extremely distressing, they are frequently under-reported and sometimes inadequately treated. Understanding some of the basic mechanisms underlying visual hallucinations in PD would not only inform treatment strategies but would improve our understanding of perceptual aberrations in general.

6.2 Review of Parkinson's disease

6.2.1 Background

Some descriptions of Parkinson's disease suggest, in addition to the characteristic motor features they display, dementia, depression, and other affective and psychotic disturbances co-exist. Other descriptions of the disease posit that the patients' mental abilities are unaffected. Communication problems and limited use of formal psychological testing have contributed to these divergent views (Goetz, 1992).

Investigations using prospectively administered neuropsychological tests did not appear in significant numbers until after the introduction of levodopa therapy. Initial studies using standardised tests assessed changes in patient's IQ functioning in response to levodopa therapy (Loranger et al., 1973). Long term improvement in IQ did not occur with this treatment. Subsequent studies have suggested that patients' visuospatial abilities were selectively impaired relative to their verbal abilities. Declines in patients' performance on tests of memory, reasoning and abstraction have also been reported (for review see Brown & Marsden, 1990)

6.2.2 Clinical Features

PD is usually defined by the occurrence of some combination of bradykinesia, muscular rigidity, resting tremor, hypokinesia, akinesia, and/or postural instability (Gibb, 1992; Marsden, 1994). Patients with PD may also manifest cognitive, sensory, and autotonic disturbances. Tremor is the best-recognised symptom of PD. Defined as the rhythmic mechanical oscillation of a body part (Findley, 1993), it affects approximately 70% of patients (Marsden, 1994). It typically begins unilaterally,

increases with stress, disappears when patients are asleep, and usually involves the extremities, face, lips, and sometimes the chin (Stacy & Jankovic, 1992).

The rigidity, which causes patients' stiffness, is a condition in which muscle tone is increased in both agonist and antagonist muscle groups. It can be increased by stress or by contralateral voluntary movement. Rigidity contributes to a slowing of movement, but is distinct from bradykinesia, a symptom believed to reflect impairments in motor program retrieval (Stacy & Jankovic, 1992). Bradykinesia is responsible for much of the delay and slowed execution of movements observed in PD patients (Marsden, 1989). It may also be related to observed difficulties in the execution of simultaneous and sequential movements.

As the disease progresses, patients often begin to display additional motor symptoms. These may include postural instability, falling, gait difficulties with absence of arm swing, and speech problems, all of which may result in part from prolonged exposure to levodopa therapy. In most patients this treatment is initially effective in reducing or eliminating motor symptoms for the duration of each dose administered. However, within five years of commencing treatment most patients exhibit fluctuations in their response to levodopa. Symptoms of motor disability initially controlled by the treatment may begin reappearing as each dose "wears off". Though initially controlled by careful timing of levodopa intake, these fluctuations can become abrupt and unpredictable, leading to periods of fluctuating mobility.

6.2.3 Mechanisms and neuropathology

The basal ganglia are a group of grey matter structures in the brain surrounding the thalamus beneath the cerebral cortex. Though their mechanisms of functioning are

largely unknown, they are believed to modulate and facilitate various motor and cognitive programs. Basal ganglia structures involved in controlling movement include the caudate nucleus and putamen (collectively referred to as the striatum), the external and internal segments of the globus pallidus, the subthalamic nucleus, and the substantia nigra (both the pars compacta and the pars reticular) (Young & Penney, 1993).

In the absence of drug provocation, motor symptoms of progressive PD are almost always related to loss of dopaminergic nerve cells in the substantia nigra pars compacta. PD resulting exclusively from damage to this site requires a loss of at least 60% of the pars compacta nerve cells. Damage to other aspects of the basal ganglia is also occasionally seen, but concurrent pathology in the substantia nigra invariably coexists. Hence, PD is predictive of pathology in the basal ganglia in general and in the substantia nigra in particular. Ultimate post mortem diagnosis of PD disorders is based on pathologic criteria that include neuronal morphology in the substantia nigra pars compacta and the distribution of nerve cell loss elsewhere in the nervous system (Gibb, 1992). The only significant macroscopic pathology in PD (in the absence of dementia) is the degeneration of the normally grey-black strips of the substantia nigra lying astride the midbrain. Microscopic examination also reveals Lewy body inclusions in a portion of surviving cells. The associated Lewy bodies are filamentous objects that signify neuronal degeneration. They appear in the early stages of the disease process and are found even before significant cell loss is apparent. Mechanisms of their formation are unknown, but it has been hypothesised that their accumulation reflects a deranged energy-dependent process involved in the transport of cytoskeleton within neurons. In most cases these inclusions are numerous, and

definite post-mortem diagnosis of PD can be ruled out if they are absent. Indeed, PD can be thought of as a manifestation of Lewy-body disease (Gibb, 1993).

Assessing the association between neuropathology and cognitive change in PD is complicated by the need to consider confounding correlates of cerebral degeneration. For example, Jellinger et al., (1984) indicated that brain atrophy in PD is more closely associated with ageing than with duration of the disease. However, limited pathogenic comparisons suggest greater severity of cell loss in the substantia nigra of younger patients (Gibb & Lee, 1988). Their finding also suggests that the activity of the disease process does not vary according to patient age.

6.3 Visual Hallucinations in Parkinson's Disease

As detailed, many known psychiatric and neurological disorders have been associated with the presence of visual hallucinations, which have been considered an integral part of the disease process. However, the presence of visual hallucinations in PD has been considered secondary to the major motor dysfunction and not as a primary manifestation of the disease processes. Specifically, PD has been associated with significant behavioural changes throughout the course of the disease with mild to moderate dementia occurring in 30% of the patients (Libermann et al. 1979).

Psychiatric disturbance in PD such as auditory (Inzelberg et al., 1998) and visual hallucinations (Moskovitz, et al., 1978) can be a frequent and disturbing complication of therapy. It is estimated that up to 33% of PD patients undergoing long-term treatment will have visual hallucinations during the course of their illness (Sweet et al., 1976; Celesia& Barr, 1970; Sanchez-Ramos et al., 1996). Although visual hallucinations are sometimes experienced in PD patients before any drugs have been

taken (Rabins, 1982), most authors report that the phenomena are related to treatment, and have been described with all anti-parkinson's medication (Celesia & Barr, 1970; Dallos et al, 1972; Sweet et al., 1976; Goodkin, 1980; Broe, 1982).

Anticholinergic agents have been clearly recognised as responsible for the occurrence of disturbances such as mental confusion in the elderly (De Smet et al., 1982) and the relationship between cholinergic and seronergic systems has recently been implicated in the occurrence of hallucinations (for review see Steckler & Sahgal, 1995). Dopamine agonists are also reported to be associated with the experience of hallucinations (Harvey, 1986). Although hallucinations are presumed to relate to central hyperdopaminergic function (Mellers et al., 1995), until recently no pharmacological study had ever tested the basic relationship between high plasma levodopa levels and the presence of hallucinations. Last year, however, a group carried out such an investigation (Goetz et al., 1998). In this study, five nondemented PD patients with daily hallucinations were given high dose levodopa infusions. The trials, which included placebo administration and patient blinding, showed that no hallucinations occurred, either with steady or pulse infusion of Levodopa. The authors suggest that the pharmacology of visual hallucinations do not simply relate to high levels of dopaminergic stimulation.

While levodopa and anticholinergic medication seem to be implicated in the aetiology of visual hallucinations, other factors that predispose patients to visual hallucinations such as dementia and advancing age have not yet been delineated. Increased age has been associated with the presence of hallucinations (Nagano et al., 1986; Tanner et al., 1983) as has cognitive decline (Meco et al., 1990). In addition, some studies exclude

patients with significant dementia (Moskovitz *et al.,* 1978), while others do not (Nagano *et* al., 1986). Since patients with dementia, of either the Alzheimers (Brabbins, 1992) or Lewy body type (McKeith *et al.,* 1992), also experience visual and auditory hallucinations, it is important to question the presence of these degenerating conditions in PD patients when investigating hallucinations. Furthermore, since visual pathology, such as cataracts or macular degeneration, can be associated with visual hallucinations (Berrios & Brook, 1984; Holroyd *et al.,* 1992), and progressive deafness can be associated with auditory hallucinations (Hammeke *et al.,* 1983), it is essential that clinical samples be assessed for such peripheral pathology which might predispose individuals to hallucinatory experiences.

Other factors that have been reported to contribute to the presence of visual hallucination in PD include psychosis, sleep disturbances, depression, levodopa treatment and dementia (for review see Manford & Andermann, 1998). Wilson et al., (1986) point to poor cognitive performance in patients who suffer from visual hallucinations compared to those who no longer have them, or have never hallucinated. Alternative personality profiles as measured by the Minnesota multiphasic personality inventory have been implicated in the identification of hallucinating PD patients (Glantz et al., 1986;Todes & Lees, 1985), suggesting the battery may be useful in predicting hallucinations in the undeteriorated parkinsonian patient.(Bonifati et al., 1990).

A self-report screening questionnaire was used by Haeske-Dewick et al., (1995) to discriminate patients who experienced visual hallucinations from those who do not. This study found that age, disability stage, self-reported loss and cognitive decline

were significantly greater in those experiencing hallucinations. Premorbid intelligence, daily levodopa intake and the use of other anti-parkinsonian medications were not factors discriminating those with visual hallucination from those without. One further interesting finding from this study expands upon the self-reporting of visual hallucination in PD. The questionnaire data resulted in a false negative ratio of 25.93%. Of the patients completing the postal screening questionnaire 10 (23.3%) reported having hallucinations. However, at interview, 16 (44.4%) patients were classified as hallucinating. Thus, it is evidence that some self-report questionnaire findings may not give a accurate incidence of visual hallucinations in PD, and as such caution must be exercised when interpreting the results of such studies.

A recent study has looked at the combination of clinical, demographic and cognitive correlates of visual hallucination in PD (Graham et al., 1997). Graham and colleagues identified two subgroups of patient with PD experiencing hallucinosis. In patients with a disease duration of five years or less, visual hallucinations were associated with rapid progression of the motor component of the disease but not the cognitive component. In contrast, patients who had suffered from PD for longer than five years, visual hallucinations were associated with postural instability, global cognitive impairment and the lack of depressive effect. They conclude that visual hallucinations were more prevalent when they were treated with a direct dopamine receptor agonist and the phenomenon was not associated with age.

In a hospital-based study, twenty nine PD patients with visual hallucinations were compared with 58 PD patients matched for age and disease duration without visual hallucinations (Klein et al., 1997). This study concluded that patients with visual

hallucinations had more frequent sleep disturbances and greater dementia. A follow-up examination of the patients also indicated that persistence of visual hallucinations was not associated with a higher rate of nursing home placement, as suggested by Goetz & Stebbins, (1993; 1995). Although this study did not offer any "new" treatment recommendations it emphasised the introduction of atypical neuroleptics such as clozapine (Musser & Akil, 1996), and olanzapine (Wolters et al., 1996) in the treatment of visual hallucinations.

The first community based study of psychotic symptoms in PD (Aarsland et al., 1999) does perhaps give unique epidemiological data on visual hallucinations. Aarsland and colleagues studied a total of 245 patients in Norway with PD, 235 (95.9) of whom participated in the study. Of these, 23 patients (9.8%) had hallucinations with retained insight, and another 14 patients (6%) had more severe hallucinations and delusions. Clinical evaluation consisted of a neurological examination and assessment for dementia and cognition. The study concluded that psychotic symptoms were more common in the late phases of the illness, and that dementia, depression, and severe motor changes were all more common in patients with hallucinations and delusions. Accordingly, the coexistence of these symptoms in patients, points to wide spread brain changes involving several neurotransmitter systems which may underlie the emergence of hallucinations in patients with PD.

As highlighted, the genesis of visual hallucination in PD remains unclear but the drug treatment, dementia and depression have been strongly implicated. Another possibility, however, which has not been systematically explored, is that severe

deficits in perceptual ability are critical for the hallucinatory experience, or that a combination of perceptual deficits with intact imagery are a prerequisite.

6.4 Rationale and Aims of Study

It is important to establish the properties of hallucinations associated with PD in order to determine how the hallucinations associated with this condition are similar to or different from normal visual perception, other hallucinations, and other quasi-visual experiences such as imagery or dreaming. This knowledge, in turn, may shed light on the cause of hallucinations as well as provide clues about the nature of visual perception in general.

Recently, Walter et al., (1990) attempted to classify hallucinations by looking for differences in activity in various brain regions when a group of hallucinating psychiatric patients was compared to a group of hypnotically induced "hallucinating" normal subjects. Using PET, they found differences in nine brain areas, including thalamic and hippocampal regions and proposed that these differences provide the basis for a classification of hallucinatory phenomena.

There are many difficulties designing and executing clinical experiments on hallucinations. First, there are no adequate animal models of hallucinations, so studies must be empirically conducted in consenting humans. Moreover, data acquisition depends largely on patient reports, and demented patients who hallucinate cannot be easily studied. Unlike hallucinating Alzheimer disease patients, many PD patients are not significantly demented and it for this reason that studies on hallucinations are feasible in PD.

When pursuing a phenomenological approach to classifying hallucinations, one must recognise that knowledge of the cause or causes of hallucinations does not follow directly from the data. Here speculation on aetiology depends upon the ability to create links between observed regularities in hallucinatory properties and theoretical models based on known brain physiology. When the phenomenological method is utilised, it is important to note that the final conclusions depend upon the questions asked of the subject. When an inquiry is made with regard to a particular hallucination property, such as whether the hallucination contains colour, that question creates a "dimension" on which the hallucinations may be placed. This in turn raises the issue of what are the relevant dimensions. What questions should be asked of hallucinators in order to characterise them? The answer is not simple. In fact, a body of literature has been written, in which aspects of a wide variety of quasi-visual experiences, including hallucinations, are examined (see Galton, 1883; West, 1962). A review of these largely philosophical and anecdotal explorations is beyond the scope of this thesis and will not be addressed here.

In a review of the visual hallucination literature, Manford and Andermann, (1998) found that a number of PD hallucinators experienced the phenomenon in the evening, occupying any part of the visual field and lasting a few minutes. Others have associated hallucinations with sleep disturbances, vivid dreams and episodes of altered arousal. The extent to which the variability of the hallucinatory experience, as described in the review papers, is due to information coming from a wide range of sources is unknown.

The research reported in this thesis aims to describe the characteristics of those hallucinations experienced in PD and determine some of the predisposing factors. Initially, a self-report questionnaire screened a sample of PD patients for the presence of current hallucinatory experiences. Individuals who consented were then interviewed to gather more detailed information about patient characteristics and features of the hallucinations. Finally, in chapter 7 a battery of neuropsychological tests designed to specifically evaluate visuoperceptual, imagery and source monitoring abilities were undertaken to compare matched groups of PD patients with and without visual hallucinations.

6.5 Methods

6.5.1 Questionnaires

Investigators at the Institute of Psychiatry and collaborators at Reading University compiled the initial questionnaire. All questionnaires were either mailed to subjects or distributed at local PD meetings. The first questionnaire was a typed A4 booklet and investigated general visual changes in PD (see appendix B1). The front page contained information about the general nature of the study, and what was required of the respondent. The first section of the booklet was used to record details of age and sex of respondents. The existence of chronic diseases and use of medication, including dosage, were recorded. Tables were provided with space to report details of up to three illnesses and drugs, if necessary. Other questions in this section referred mainly to PD symptoms and possible anti-Parkinsonian medication, but they were designed in such a way that a non-sufferer could answer them (e.g. 'Do any of your limbs feel rigid?'). This section also asked about the possible occurrence of tremor and akinesia, difficulties with walking through doorways, and 'freezing' episodes.

Respondents were also asked about the occurrence of fainting, migraine or motion sickness. These questions in the first section of the questionnaire were designed specifically for a study at Reading University and the responses played no part in this investigation.

The second section of this questionnaire was used to record information about changes in vision, such as changes in appearance ("Do familiar things around you ever appear to change their appearance unnaturally in some way?"); hallucinations ('Do you ever see things that are not really there?") and the properties of these phenomenon, such as motion ('Do these images move?"). The second questionnaire was administered to participants who answered "yes" to either "Do familiar things around you ever appear to change their appearance unnaturally in some way?" or "Do you ever see things that are not really there?" and the same number of subjects who responded "no" to these questions, in an attempt to recruit a non-hallucinating PD control group.

The format of the second questionnaire was an A4 booklet with section one asking about personal details and section two asking specific questions on visual disturbances. (see appendix B2). It was hoped that the presence of visual disturbances would be a good indicator that the subject had experienced hallucinations, and subsequently if visual hallucinations can be found to exhibit a common set of properties, then those properties may in turn shed light on the processes that create the hallucinations. The questionnaire was constructed to form an independent sample and it was not dependent on the answers given in the first questionnaire. Section one again asked for personal details including age, sex and medication while section two was

constructed to give information on the nature and properties of the subject's visual hallucinations. The questions asked about the hallucinations derive from four broad "dimensions." The dimensions examined do not represent an exhaustive set, but sample a wide variety of properties, including temporal factors (frequency, duration, onset), content (quantity, colour, clarity, movement), subjective concomitants (affect, arousal level, perceived control), and external factors (triggers, state of eyelids). The aim of the analysis was to determine the experiential properties of these hallucinatory episodes.

6.5.2 Subjects

Two groups of subjects took part in the study. Subjects were putative sufferers from PD. Individuals were assigned to groups according to whether they had experienced visual hallucinations in the last three months, and those who had never experienced visual hallucinations. Respondents were recruited through the questionnaire study with University of Reading, at local branches of the UK Parkinson's Disease Society, and at a neurology clinic at the Maudsley hospital. A limitation of this recruitment procedure is that the normal and PD subjects were essentially self-selected and this might have biased the completion of questionnaires towards those with visual problems. Finally, no patient in the population sampled had either a diagnosis of Alzheimer's disease or a clinical diagnosis of Lewy body dementia.

From the initial questionnaire study, 182 replies were received, and of these 31 (17.2%) reported the presence of visual hallucinations within the last three months. Of the 31 patients experiencing hallucinations, 24 were willing to answer the second

questionnaire on visual disturbances and take part in the neuropsychological study. A control group of 23 patients without hallucinations was also recruited.

6.5.3 Demographics

It was found that the hallucinating (n = 24, of whom 10 were male) and non-hallucinating (n = 27, of whom 12 were male) groups initially did not match in age. However, subjects who reported frequent migraines (hallucinators = 2, non-hallucinators = 2) and eye disease (hallucinators = 1, non-hallucinators = 2) were excluded. This left 21 questionnaires from hallucinators (7 of whom were male) and 23 questionnaires from non-hallucinators (of whom 9 were male). The non-hallucinator group had a mean age of 63.23 years (SD = 10.82 years) and the hallucinator group had a mean age of 67.62 years (SD 6.52 years). The two groups differed significantly on illness duration ($t(42) = 2.34$, $p < 0.05$), but did not differ in age ($t(42) = -1.615$, $p > 0.05$), or L-Dopa medication ($t(42) = 1.887$, $p > 0.05$).

Table 6.1
Subject Demographics

	Hallucinators	Non-Hallucinators
No.	21	23
Gender: Male Female	 7 14	 9 14
Age: (mean yrs)	67.62 (SD 6.52)	63.23 (SD 10.82)
Length of Illness: (mean yrs)*	11.76 (SD 5.42)	8.30 (SD 4.38)
Daily levodopa (mg)	578 (SD 163)	670 (SD 159)

* $p < 0.05$

6.6 Results

Brief details of the hallucinatory experience are detailed for each case in table 6.2. The percentages of each group who reported the presence of problems or symptoms can be found in table 6.3.

Table 6.2
Hallucinations associated with Parkinson's disease in 21 patients

Patient No.	*Sex*	*Age*	*Description of Hallucinations*
1	M	75	Dead relatives walking about the house. See his dead dog by his bed
2	F	64	People, in old style dresses. Some disembodied figures. Bright circle that change into small children
3	F	65	Egg shapes that move around. See dogs and cats on the sofa
4	M	75	Humans sitting in lounge. Children playing in garden
5	F	76	Shadows of figures approaching here from behind. Molecular structure of materials. Small girls looking in through the window
6	F	55	Spiders in her bed
7	F	65	People sit in Kitchen
8	M	64	People in garage. Big heads. Small girls and soldiers
9	F	66	Blackbirds sitting on shoulder
10	F	72	A flight of stairs appears in the garden. Spiders in her tea cups
11	F	64	Shadows, not very clear. See animal and birds when turning head
12	M	68	Spiders and piles of hairs around the house
13	F	77	Dogs face and people walking around the house
14	M	61	Brick red images of faces. Patterns covering buildings. Birds flying about
15	F	68	Small insect running around on the table. People in rooms as she walks past and looks in.
16	M	68	Vague human forms which she sees over her shoulder. Disappears when he looks around
17	F	71	Insect and spiders on duvet. Patterns on walls, which move in and out of the wall. Waterfall coming out of wall
18	F	69	Signposts change into men. Holes appear in carpet which go into the earth. Children's faces with distorted features.
19	F	73	Legs underneath trees in the garden. Small dogs and cats chasing each other around the house.
20	M	52	Black shadows moving around, sometimes change into human forms
21	F	72	Children by televisions set late at night. Small girls messing around in her kitchen cupboards. Bleeding face on wall

Table 6.3

Characteristics of visual hallucinations in 21 patients with Parkinson's disease

	Hallucinators	
Variable	**Number**	**Percentage**
Frequency of Hallucinations		
>5 per week	5	23.8
1 to 5 per week	8	38.1
<1 per week	8	38.1
Form		
Yes	16	76.2*
No	5	23.8
Onset		
Sudden	16	76.2*
Gradual	5	23.8
Duration		
Hours	1	4.8
Minutes	7	33.3
Seconds	13	61.9*
Movement		
Present	18	85.7*
Absent	3	14.3
Number of Images		
One	15	71.5*
One to Five	4	19
More than Five	2	9.5
Clarity		
Sharp	3	14.3
Blurry	11	52.4*
Transparent	2	9.5
Variable	5	23.8
Perceived Control		
Have control	7	33.3
No control	14	66.7

	Hallucinators	
Variable	**Number**	**Percentage**
Colour		
Black and White	7	33.3
Single Colour	6	28.6
Multiple Colours	8	38.1
Eyelids		
Open	21	100*
Closed	0	0
Reality		
Seemed Real	13	61.9
Seemed Unreal	8	38.1
Lighting		
Bright	5	23.8
Dim	11	52.4*
Dark	3	14.3
All Conditions	2	9.5
Trigger		
Starts with Percept	12	57.1
Starts Independently	9	42.9
Medication Related		
Yes	5	23.8
No	16	76.2
Content		
Stereotyped	7	33.3
Different	14	66.6
Field of Vision		
Complete	2	9.5
Partial	19	90.5*
Distortion of image		
Present	8	38.1
Absent	13	61.9

* $p < 0.05$

The distribution of responses obtained for each question was subjected to a Chi-square test to investigate whether the distribution of answers was achieved by chance alone (see table 6.3). The frequency of the hallucinatory episodes varied among the respondents. Just over three-quarters of the patients had five or less hallucinations per week (76.2%). Only in 5 cases did the hallucinations occur more than five times a week. In all cases patients had their eyes open while experiencing the hallucinations.

The duration of the experiences reported varied according to the time of day that the hallucination manifested, with the longer episodes occurring either in the morning or evening. Although the term "minutes" was intended to indicate an experience that lasted minutes, some of the patients classified their hallucinations as lasting ninety minutes or so, and not hours. This clearly may have lead to ambiguity in the responses. However, at interview, clarification was sought on the answers to this question and recoded. In one patient, hallucinations lasted several hours and manifested gradually through the day. The remainder claimed that their hallucinations generally lasted for a few seconds up to 30 minutes. Less than a quarter of the patients had hallucinations that appeared gradually and less than 10% found that the hallucination completely filled their field of vision.

It has been reported that all dopaminergic medication may evoke hallucinosis, however, there is dispute over which class of medication is most likely to do so (Cummings, 1991). In this study, the hallucinations did not show a clear relationship with medication. In only 5 cases (23.8%) were the hallucinations reported to relate to drug intake. This relationship was established because of the onset or aggravation of the mental symptoms. In 16 cases (76.2%) subjects claimed their hallucinations were

not linked to their medication. In those patients, seven of them hallucinated in their immobile periods, usually at night or first thing in the morning.

There was a difference in the reported colour of the hallucinations. Seven patients experienced black and white images while 14 had single colour or multiple colour hallucinations. The clarity of the hallucinations was blurry in 11 (52.4%) of the 21 cases, transparent in 2 cases (9.5%) and variable in five cases (23.8%). Only five patients (14.3%) described their hallucinations as sharp. In all of these 5 cases the hallucinations were of meaningful content, pets or loved ones who were now dead, where perhaps the familiarity of the object as an earlier perception may have contributed to the clarity of the hallucination. Although in most cases the hallucinations were not sharp, 13 patients (61 %) claimed their hallucination seemed real to them. Sixteen of the subjects (76%) reported having hallucinations that had form. Often the content was mundane such as an animal or unfamiliar person but did range to the bizarre (faces made of brick). The variety of animals reported included horses, cats, dogs, rats and spiders. The visual hallucinations involving people consisted of relatives, soldiers and "strange people" mainly involving children, particularly girls. In 15 cases (71.5%) the hallucination was of a single image. A high number of the hallucinations were dynamic with 18 patients (85.7%) reporting movement. Fourteen patients (66.6%) reported that the hallucnations were not recurrent and that the images were different rather than stereotyped. Seven patients (33.3%) however had recurrent hallucinations generally in the same surroundings. These hallucinations are as one patient put it "similar to a video recording of an event, which replays everyday".

The impact of the environment had an effect on the occurrence of hallucinations, with 11 patients (52.4%) reporting that their experiences only happen in dim lighting conditions, while 5 patients (23.8%) reported hallucination in bright conditions. Only 2 patients (9.5%) reported that their hallucination happened in all lighting conditions while three patients (14.3%) only had them in the dark.

Fourteen (66.6%) described their experiences as involuntary, in that onset or termination was not related to any particular action or thought on the part of the patient. Some relatives, however, reported that intellectual exercise and distracting stimuli, such as watching television, seemed to terminate hallucinatory episodes. The seven patients (33.3%) who did have control of their hallucinations, were only able to terminate the image. The most common way of interacting with the hallucination was either by walking towards it or by trying to touch it. Twelve patients (57.1%) reported that the hallucination started with a percept that slowly changed into another image, while the remainder stated that the images appeared independently. It was found that 13 patients (61.9%) had no distortion of the image(s) in the hallucination. Emotional responses at interview were varied, often in line with the severity of the hallucinations experienced. Frustration, anger, fear, and in a few cases indifference were the responses experienced. Two clinical cases are presented as examples to illustrate the experiences of the patient and the properties of the hallucinations.

Case 01

Female: *Born 1921*

This 77-year-old woman has had PD for 20 years. The subject reported that she woke up one morning in 1997 experiencing different visual phenomena, ranging in complexity and apparent type. In 1998, she began to experience very realistic-looking hallucinations of two dogs, when she watched television. The subject noted that the images, when they appeared, gradually formed on the television screen after watching it for 15 to 30 minutes. Each dog's eyes appeared first, then its nose, mouth and the remainder of its head. She reported that one was a beige-coloured spaniel and the other an Airedale with a dark patch on its back. The subject reported an irregular sleeping pattern, waking in the middle the night, or at an early morning hour. At these times the subject reported getting out of bed and having a cup of tea before going back to bed. One of the complex, well-formed images that she had experienced on one occasion is the figure of a man. She describes the image as tall, thin, and very beautiful to look at. The figure was monochromatic and was further described as being very neatly dressed in a black suit with a grey shirt. He had long black hair with grey streaks in it. The subject reported not being able to see his face. This hallucination was estimated to last for 3 minutes. When she attempted to wake her husband, the figure walked around the room then rose slightly in the air and receded back through the wall of their bedroom. She said that she saw a similar figure again, on a separate occasion, from the torso up as if it was kneeling. She further said that a couple of months prior to interview, again at night, she saw a very clear image of her mother by her bed.

Case 02

Male: Born 1937

Subject 2 was a 61-year-old man who had had PD for 7 years. His hallucinations started approximately 18 months prior to interview. Since that time they had occurred almost daily. His principal hallucination consisted of seeing a brick-red image of a face. The face did not look real but more mask-like with the eyes closed. The image appeared almost everyday, with each hallucinatory episode lasting between 10 and 15 minutes. The subject's most recent hallucinatory episodes consist of seeing the mouth area of a face. The image always appeared in the late afternoon when he attempted to relax but was emotionally upset. He described two versions of the mouth, one being pleasant to look at and the other unpleasant. The "nicer" image was composed of a pair of thin lips with the mouth closed. The nose could be seen, but part of the chin was present. The image appears in natural copper-coloured flesh tones. In contrast, the unpleasant mouth is larger and had a deeper copper colour. The lips were thicker and slightly parted almost in a grin, exposing three teeth. In addition, subject 02 reported three other unusual visual experiences. When outside, subject 02 saw one particular building covered in what looked like small lilacs, though he knew that it was not. This covering "appeared thicker than moss" and was greyish-brown in colour. Other buildings in his neighbourhood did not have this appearance. Subject 02 also reported that when he mixed porridge in the morning he saw a brownish granular substance in the pot. This often made him think that the porridge was contaminated, although his wife, upon inspection of the breakfast, found nothing. Finally, at the second interview, the subject amusingly related a recent hallucinatory experience when he and his wife attended a play. At a point during the play the subject noticed black coloured birds fly out into the audience. The subject marvelled at the "special effects" provided during

the play. It was only later, when talking to his wife, that he discovered that they were not real.

6.7 Discussion

There are implicit difficulties designing and executing investigations on hallucinations. In contrast to hallucinating Alzheimer's patients, many PD patients are not significantly demented, and may actively contribute to studies on visual hallucinations. We found that our subjects were particularly eager and willing to participate in this research program.

This investigation indicated that hallucinations associated with PD seem to exhibit a common set of characteristics. The typical hallucinator's experience occurs while alert and with his/her eyelids open, generally in dim surroundings. It involves having a blurry image appear suddenly without voluntary effort, filling an area of the visual field. The hallucination is present for a few seconds, typically moves while present, and then suddenly vanishes.

A notable observation from the data was that the most severe hallucinations, i.e the ones that were minutes and hours in duration together with clear images, were exhibited by six of the patients who were the oldest (mean 71.67 yrs, SD = 3.56) and on medication the longest (mean 14 yrs, SD = 4.49). It has been generally supposed that hallucinations in parkinsonian patients occur as a side effect of drug therapy (Celesia & Barr, 1970; Sweet et al., 1976). However, hallucinations were reported be-fore the use of L-dopa and anticholinergic drugs (Rondot *et al.,* 1984) and have been reported in patients affected by diffuse Lewy body disease (Gibb *et al.,* 1987). While

reduction in levodopa and anticholinergic medication doses has been recommended in the management of hallucinations (Sanchez-Ramos et al., 1996), more than 75% of patients in this study did not attribute their hallucinations to the medication they were taking. In follow-up interviews, seven of the patients reported having hallucinations while immobile, adding further support to their claim. Recently, it was reported that visual hallucinations do not simply relate to high levels of levodopa (Goetz et al., 1998). Hallucinations may occur not because of the level of medication but the duration of the medication, and instead may be related to the underlying pathology in the cerebral cortex. Indeed, recent work has shown that Lewy bodies are present to a greater or lesser degree in all cases of PD (Hughes *et al.,* 1992).

Many arguments have been postulated to explain why increased age may be associated with the experiencing of hallucinations in PD. Ageing can be associated with hallucinations, particularly when visual disturbances are present (Brown, 1985). Age-related side effects of medication can be a factor in PD (Pederzoli et al., 1983) and ageing was a risk factor for hallucinations in our patients. Since increased age is associated with increased sensory loss, it might be hypothesised that poorer sensory functioning might be predisposing older patients to hallucinatory experiences, as confirmed elsewhere (Berrios and Brook, 1984; Holroyd *et al* ,1992).

The findings from this study concur with previous investigations. The visual hallucinations most frequently reported were complex, usually containing animate or inanimate object or persons (Haeske-Dewick, 1995). Usually they contained five or less images and sometimes were meaningful to the individual. For example, one man regularly saw his dog, which had died five years earlier, lying by the bed. In addition,

most reported that their hallucinations often occurred in dim surrounding, were non-threatening and were sometimes recurrent (Moskovitz et al., 1978).

The hallucinatory process and perhaps the normal perceptual process, involves satisfying "epistemic hunger' with a mechanism that reports on information gathered from the environment (Dennett, 1991),. The brain generates hypotheses, then has them "accepted" or "refuted" on the basis of information from the environment. Looking at how the properties of hallucinations found in this study differ from those of normal visual perception, we can see that the hallucinations are unlike normal perception in that the hallucinations are only present for a brief time and are generally blurry in nature. The hallucinations also seem particularly susceptible to being identified as hallucinations when they are actively examined. Perhaps as time passes during examination, the likelihood that the hallucination conforms precisely to what is anticipated becomes increasingly small. Thus, the hallucinations are present for only brief periods. Anecdotal evidence is consistent with this account. Indeed seven of the hallucinating subjects who had "control" of their experiences reported that the hallucination disappeared when the hallucinator approached the hallucination or attempted to interact with the hallucinated object.

The fact that these experiences can occur with little or no information from the environment argues strongly for "top-down" processes playing a role in the production of the hallucinations. Neisser (1976) argues convincingly that perception is a cyclical process involving receiving information from the environment through cognitive schemata which in turn direct exploration for new information. Most relevant here is Neisser's notion of anticipatory schemata. Anticipatory schemata are

"cognitive structures, that prepare the perceiver to accept certain kinds of information rather than others and thus control the activity of looking". Accordingly, hallucinations in PD may occur when an anticipatory schema is activated.

All the patients in this study retained insight into their condition. Even though some of the images appeared real, subjects "knew" they were hallucinating. Although a visual event could seem to take place externally to an individual, not be under voluntary control, the individual can still have the "phenomenological feel" of their own mental processes. Hence, the hallucination may be termed a "pseudo-hallucination", since the visual experience is very vivid and non-controllable (as is normal visual perception) yet can be distinguished from normal visual perception in that it occurs in an imaginal space. A judgement can thus be made that the experience is not real.

It is also paradoxical that phenomenology is both a strength and weakness of psychological research, for it seeks to classify the subjective "what it's like" to have uniquely human experiences, but does not allow the objective verification of its data. When combined with the fact that language can, in some instances, fail to adequately describe our experiences, confusion may arise as to what a word or phrase means in experiential terms. Researchers (Aggernaes 1972), for example, have attempted to determine how realistic schizophrenic hallucinations are by having schizophrenics rate their hallucinations along seven rather similar dimensions such as: sensation vs. ideation, publicness vs. privateness, objectivity vs. subjectivity, existence vs. non-existence. In the present study, attempts were made to query a variety of properties of visual hallucinations. Where possible, respondents where interviewed and talked

through their experiences. It was this approach, combined with the questionnaire data, which gave a more accurate picture of the hallucinatory properties.

6.8 Conclusions

The hallucinations in PD, like all higher-order perceptual phenomena, are obviously very complex. Visual hallucinations in the patient with PD probably result from a complex interaction of many factors, including cognitive, affective, medication, and even environmental factors. Typically, the hallucinator's experiences occur while he/she is alert and with the eyelids open. Moreover, an image appears suddenly, without any apparent trigger or voluntary effort. The hallucination is present for a few seconds or minutes, generally moves during this time, and then suddenly vanishes. With regard to the mental status of the hallucinators, the consensus based on case reports has been that the hallucinators are not psychotic, nor are they, by and large, cognitively impaired. Nevertheless, in this study, their psychological status has not yet been addressed systematically using formal psychological tests. The next study addresses this question systematically and examines the mental status of the hallucinator utilising tests to investigate visual perception, visual imagery and source monitoring capabilities.

Chapter 7: Recognition Memory, Source Monitoring and Visual Hallucinations in Parkinson's Disease

7.1 Introduction

Memory traces may constitute the building blocks of hallucinations, as they do in dreams. Indeed, it has been theorised that hallucinations may be the result of abnormalities in the memory retrieval system (Jarvik, 1970). Some have suggested that hallucinations occur in certain people because of abnormalities in the imagination process related to either enhanced vividness or an imagery deficit (Starker & Jolin, 1982).

Memories derived from imagination can be vivid and detailed, sometimes leading people to mistakenly believe that events that were only imagined actually had occurred. Errors of this sort range from minor confusions, such as mistakenly believing you did some particular task when you only thought about doing it, to remembering that you saw a particular object when you only imagined it. *Reality monitoring* refers to the processes involved in discriminating between these types of external and internal sources of information (Johnson & Raye, 1981).

7.2 Reality Monitoring and Visual Hallucinations

7.2.1 Reality monitoring deficit?

As briefly mentioned in chapter 1, Mintz and Alpert (1972) suggested that hallucinations might arise as a result of failed reality monitoring combined with vivid imagery. They screened hallucinating schizophrenic patients, non-hallucinating patients, and normal controls on Barber and Calverley's (1964) "White Christmas"

test. In this test, subjects are invited to close their eyes and imagine "a record with words and music playing "White Christmas". They are asked afterwards to decide which of four descriptions best matched their experiences: a) They heard the record clearly and believed it was playing: b) They heard the record clearly but knew that no record was playing: c) They had a vague impression of a record: d) They heard nothing.

Mintz and Alpert found that 17 of 20 hallucinating schizophrenics opted for option a or b, but only 1 out of 20 non-hallucinating subjects did so. Rather less than 50% of control subjects opted for b (none for a), a slightly lower proportion than had been reported by Barber and Calverley in their original study, though this may be explained by slightly different instructions issued in the original study.

Mintz and Alpert then went on to test the same patients in a speech perception experiment where subjects had to report which words were played in different amounts of white noise, and report their confidence in their reports. For normal subjects and non-hallucinating patients there was a clear correlation between confidence and accuracy. When the words were most difficult to hear, people reported most uncertainty in their reports. The hallucinating group showed a much weaker correlation. This suggested to Mintz and Alpert that this group were failing to monitor reality properly, and it was this combined with their vivid imagery that created the combination of factors promoting hallucinations.

The relationship between hallucinations and reality monitoring deficit, defined as failure to discriminate imaginary from real events, has been directly tested by Bentall

and Slade (1985). Using an auditory signal detection task, they found that more hallucinations were correlated with an increased bias towards false alarms, in both schizophrenic patients and normal individuals prone to hallucinations. These subjects had a propensity to report as real, events that had not occurred. Recently Rankin and O'Carroll (1995) replicated this result in a sample of normal individuals prone to hallucinations. In addition, they found that these individuals more frequently reported *heard* words that had only been *imagined.*

It has also been suggested that hallucinations are linked to a bias towards attributing to an external source an event which had been generated by oneself (Bentall, 1990). This hypothesis has been tested in paradigms where words were provided either by the subject or by the experimenter, then the subjects were required to remember the source of these words. It was found that hallucinators had a bias towards attributing their own words to the experimenter compared with either psychiatric or normal controls (Bentall, Baker & Havers, 1991; Morrison & Haddock, 1997).

Even normal subjects tested in ambiguous circumstances can be shown to fail to discriminate reality from imagination, as in the situation described by Perky (1910). In Perky's (1910) experiments, subjects were asked to imagine a particular object (e.g. a yellow banana, or a green leaf) projected onto a smoked glass screen. While engaged in imagining these objects, pictures of the same objects were projected onto the screen, very faintly and with fuzzy outlines. Under these conditions, some subjects reported seeing clear visual images of the objects but they did not think they were really seeing the objects, even though they were.

Why did subjects in these experiments confuse reality with imagination in this way? Usually we can tell whether something is "real" or not by seeking other sensory evidence: we can reach out and touch a real but not an imagined object. Moreover, certain systematic changes in viewpoint occur as we move our eyes and head when viewing a real but not an imaginary object. Indeed, certain illusory phenomena (as opposed to imaginary ones), such as the hollow face, are revealed as illusory because they violate normal expectations when movements are made. Real objects occlude other objects in the background appropriately, and are invisible when the eyes are closed.

In experiments that followed the Perky effect, Segal and colleagues produced some evidence to support the idea that the effect depends on limited opportunity and information to confirm the perceptual hypothesis. Segal and Nathan (1964) replicated the Perky phenomenon, but a much smaller percentage of subjects confused the projected images with their own perceptions. This percentage increased with a change of apparatus so that subjects looked into a translucent cylinder that restricted their field of vision, and also their opportunity to seek better perceptual evidence. Moreover, circumstances that provided better perceptual evidence, where stimuli were more intense, of longer duration, less fuzzy in outline, or presented with a background, were less likely to be confused with imagination (Segal, 1970).

Marcia Johnson and colleagues have studied the processes that allow us to distinguish real from imagined events in memory (e.g. Johnson, Hashtroudi, & Lindsay, 1993; Johnson & Raye, 1981). The basic assumption underlying the framework developed by Johnson is that memory potentially consists of numerous attributes of physical

properties, semantic properties, contextual information about time and place of occurrence, and cognitive operations associated with the event, such as acts of image generation or effort after meaning. Johnson sees the attribution of the source of a memory to external or internal events as an act of judgement that depends on a weighing up of the balance between stored perceptual information and stored information about cognitive activities associated with these events. Her framework has been elaborated as a model: the "multiple entry modular memory system" or MEM, where two reflective subsystems (the "executive" and "supervisor") interact with two perceptual subsystems in monitoring and initiating behaviour and thought processes, which in turn deposit records of past activity within the systems themselves. Thus, the memory system preserves the results both of perceptual processing (external memories) and of the self-generated or reflective activities (internal memories) that are the properties of the executive and supervisory systems.

The previous discussion suggests that our everyday discrimination of real from thought events requires that we monitor the source of representations. It is also necessary for these different aspects of our ongoing cognition to be retained in memory, or we will be in danger of mistaking, for example, a remembered dream for something that actually happened, or an imagined object as a real percept.

Indeed, it has been suggested (Frith, 1992) that hallucinations in patients with schizophrenia could stem from a reality monitoring deficit. The theoretical hypotheses suggest that a bias toward external misattributions, which could be identified as a *'self-monitoring'* deficit, is involved in hallucinations. Whether this bias is specific to

hallucinations, as suggested by Bentall et al. (1991), or involved in other symptoms like delusions and thought disorganization needs further investigation.

It has also been proposed that older adults are less efficient at binding or integrating contextual information with a target memory (Chalfonte & Johnson, 1996; McIntyre & Craik, 1987) and that age deficits in some reality monitoring tasks result from reduced accessibility of source-specifying attributes in memory, such as perceptual detail, spatial and temporal information, and information regarding cognitive operations (Hashtroudi et al., 1990; Johnson, De Leonardis, Hashtroudi, & Ferguson, 1995). Consistent with this, older adults are less likely than younger adults to report that they consciously recollect contextual details surrounding a remembered event, although they are not necessarily impaired at knowing that the event occurred or in their confidence in the event's familiarity (Mantyla, 1993; Maylor, 1995; Parkin & Walter, 1992).

7.2.2 Recognition memory and reality monitoring

So, not only do we have the possibility of confusing imagination with perception, but we also face the prospect of confusing remembering. The products of previously imagined material may be confused with products of previously perceived material. Furthermore, discrimination of internal and external events in recognition memory may not be a unitary concept, but rather based on the possibility that recognition is a joint product of two elements: familiarity and recollection (Mandler, 1980).

Since earlier work by Mandler, there has been an increasing volume of research addressing the componential nature of recognition memory performance. The

Recognition and Conscious Awareness (RCA) paradigm originated from a phenomenological study that was designed by Tulving (1985) to address the question of whether tests, such as free recall, were true measures of explicit memory. The test involves subjects making a judgement on recognised stimuli, which aims to address their conscious states of awareness. They are asked to subdivide their "memory" for the stimulus item into a *recollective experiences* (or 'remembering') or a *feelings of familiarity* (or 'knowing'). These are termed Rs and Ks respectively. This paradigm has since been developed by a number of other researchers (e.g. Gardiner, 1988; Gardiner & Java, 1989; Gardiner & Parkin, 1990; and Parkin & Walter, 1992) who have provided supporting evidence for the theory that there are two components of recognition memory for externally perceived items. Similarly, the same two components may be discernible in the recognition of internally generated phenomena.

7.3 Rationale and Aims

As indicated, many authors have hypothesised that hallucinations are linked to a self-monitoring deficit, that is, a propensity to attribute a self-generated event to an external source. Thus, hallucinations could arise from a lax criterion for the discrimination between real and imaginary. It may be that visual hallucinations are linked to a confusion between imagination and perception, as auditory hallucinations are experienced when inner thoughts are perceived as external voices (David, 1994; McGuire et al., 1996). Accordingly, the present study involved tests to investigate the relationship between recognition and source monitoring parameters and visual hallucinations. It is hypothesied that hallucinators will rely on the "feeling of knowing" rather then "remembering" stimuli to make object recognition judgements.

Consequently, these impoverished memories will lead to poor source monitoring abilities.

In conjunction, a battery of neuropsychological tests was administered to examine general intellect and visual processing abilities. The aim was to assess the underlying "markers" of hallucinatory disturbances associated with Parkinson's disease. All tests were administered to PD patients with visual hallucinations, a similar non-hallucinating group and neurologically normal age-matched controls.

7.4. Recruitment of Subject Groups

The Parkinson's patients with hallucinations were recruited from the subjects detailed in chapter 6. Of the original 21 patients with hallucinators, 17 were willing to take part in this experiment. Non-hallucinating subjects (N=20) were recruited from the questionnaire study (detailed in chapter 6). Elderly subjects were recruited by means of opportunity sampling through local activities, educational and social groups (see table 7.1). In all cases, subjects were asked to recommend any suitable acquaintances for participation in the study. The subjects came from a variety of backgrounds, in terms of education, vocation and socio-economical status. Subjects were matched for age and pre-morbid verbal intelligence as assessed by the National Adult Reading Test (NART, Nelson & O'Connell, 1978).

The first session with every new volunteer consisted of an informal conversation where the subject was given a brief description of the research being carried out, their involvement, and the type of tasks they would be performing. It was ensured that subjects understood that they were volunteers and could withdraw at any time, and

there was emphasis on the confidentiality and anonymity of their results. This session also gave the experimenter an opportunity to assess the new subject as to their suitability for participation.

Table 7.1
Subject Demographics

	Normals	***Non-Hallucinators***	***Hallucinators***
No.	20	20	17
Gender: Male Female	 11 9	 8 12	 6 11
Age: *(mean)*	66.10 (SD 7.49)	62.75 (SD 10.93)	67.88 (SD 5.89)
MMSE: *(mean)*	29.1 (SD 0.82)	27.6 (SD 1.39)	26.71 (SD 1.10)
NART : *(mean)* *(full scale IQ)*	116.10 (SD 9.37)	111.90 (SD 8.14)	113.53 (SD 9.65)
Beck's depression inventory)**	8.9 (SD 2.59)	16.60 (SD 5.39)	18.24 (4.54)
Duration of Illness *(mean years)**		8.75 (SD 4.42)	11.88 (SD 4.27)
Hoehn & Yahr *(mean)**		2.95 (SD 0.57)	3.47 (SD 0.63)
Daily levodopa (mg)		457 (SD 276)	498 (SD 317)

*p<0.01 significant group effect between hallucintors and non-hallucinators
** p<0.001 significant group effect between normals and both PD groups

Selection of the elderly control subjects was based upon a number of criteria with regards to lifestyle and health. All the subjects lived independently in their own homes and led active lives. They had adequate vision and hearing (with correction where necessary) to perform all the tasks. Screening led to the exclusion of any subjects who had suffered from severe cardio-vascular conditions, diabetes, psychiatric disorders, eye disease, alcohol abuse, epilepsy or neurological disorders. Criteria for inclusion also included a Mini-Mental State Examination (Folstein et al.,

1975), on which all participants had to achieve a score greater than 24. For all Parkinson's patients duration of illness and medication was noted and disability stage was recorded (1-5; Hoehn & Yahr, 1967).

7.5 Neuropsychological Tests

7.5.1 Mini metal state examination (MMSE): *(Folstein, Folstein & McHugh, 1975) (see appendix C1)*

The Mini Mental State Examination (MMSE) was used to provide gross estimates of cognitive function and to detect early signs of dementia. Subjects were asked questions assessing orientation (see appendix C1), providing measures of immediate and delayed recall, attention, calculation, simple language ability, and visiographic skills. The maximum score on this test was 30, from which points were subtracted with each error, leading to a possible lowest score of 0. Scores in the range of 27-30 are usually considered normal, while scores of 22 or below suggest probable dementia (Folstein et al., 1975). In the current study, more stringent parameters were applied, leading to the exclusion of subjects who obtained below 24.

7.5.2 National adult reading test (NART) *(Nelson & Willison, 1991) (see appendix C2)*

The NART entailed counting the number of errors made by subjects when reading aloud 50 irregularly spelled words. This test is very highly correlated with the Wechsler Adult Intelligence Score (WAIS-R) Full Scale, allowing full scale and verbal IQ to be predicted. In this study, NART was used to match the subject groups on pre-morbid verbal IQ.

7.5.3 Beck depression inventory *(Beck et al., 1961) (see appendix C3)*

The 21 item Beck Depression Inventory was administered to each subject. Each question was read to the subject. If a subject endorsed the first statement in the question, the statement was checked and the next question asked. If the subject did not endorse the first statement to a question, all the remaining statements from the question were read to the subject. Higher scores indicate depressive mood. Scores greater than 10 indicate mild depression (see table 7.1)

7.5.4 The visual object and space perception battery (VOSP) *(Warrington & James, 1991):*

This battery consists of eight visual object and space perception tests (VOSP), with each test focusing on one components of visual perception, while minimising the involvement of other cognitive skills. There are four tests of object perception and four tests of space perception, the majority of which require simple responses. A brief description of each test follows, the number in the bracket indicates the maximum score available.

Shape detection screening test (20):

This is a screening test designed to establish whether patients have adequate visual sensory abilities to perform the VOSP. Stimuli consist of patterns as shown in figure 7.1, which subjects are asked to identify. The criterion set for success on this test is a score of 15, which all the subjects in this study reached, leading to no exclusions.

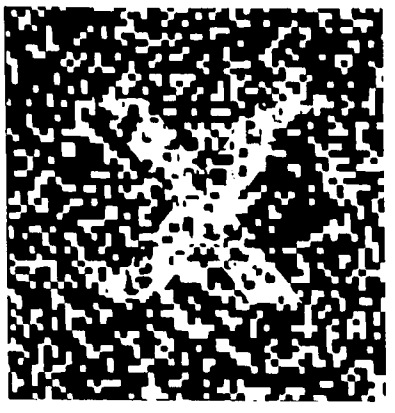


Figure 7.1
Example of shape detection screening test

Test 1. Incomplete letters (20)

The incomplete letters test consists of letters degraded by 30 per cent or 70 per cent (see figure 7.2). The test stimuli are 20 letters (70 cent per degraded) and two practice items (30 per cent degraded) which are used to explain the task. The subject is shown the items and asked to identify the letter.

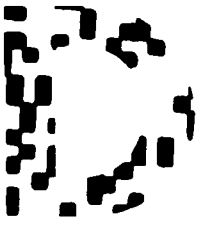


Figure 7.2
Example of incomplete letters

Test 2 Silhouettes (30)

The stimuli are silhouettes drawn from the outline of objects rotated through varying degrees from the lateral axis. The test consists of 15 silhouette drawings of animals (see figure 7.3) and 15 silhouette drawings of inanimate objects. The silhouettes of these are arranged in order of difficulty. The subject is shown the first animal

silhouette and is told that it is a drawing of an animal and asked to name it. This procedure is repeated for each silhouette and abandoned after five failures.

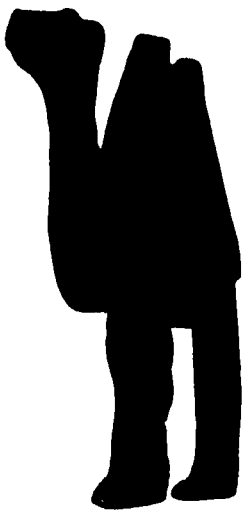


Figure 7.3
An example of an animal silhouette

Test 3 Object Decision (20)

The test stimuli consist of a two-dimensional silhouette drawing of an object together with three nonsense shapes (see figure 7.4). The silhouettes are close to an object recognition threshold and are considered minimal views. The object decision test consists of 20 arrays, each of which displays one real two-dimensional object together with three distractor items. The subject's task is to point to the real object in the array.

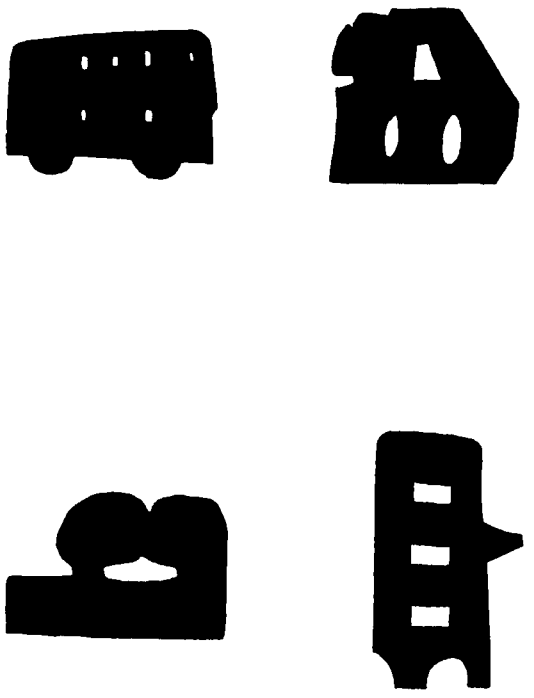


Figure 7.4
An example of the object decision task

Test 4 Progressive Silhouettes (20)

The test consists of two series of silhouettes, one of a gun (see figure 7.5) and the other a trumpet. The first silhouette of the series is presented and used to explain the task. The pages are then turned, the silhouette drawing becomes progressively easier to identify with each page. The number of trials required to identify each object are summed and recorded as a score (maximum trials = 10 +10).

Figure 7.5
An example of the gun silhouette at positions 5 and 9

Test 5 Dot counting (10)

Each stimulus consists of an array of black dots on a white card (see figure 7.6). There are 10 arrays consisting of two each of five, six, seven, eight and nine dots and each array is arranged to form a random pattern. The maximum distance of a dot from the centre of a card is 120mm and the minimum distance between dots is 10mm. The first array is used to explain the task. The subject's task is to report the number of dots on the card.

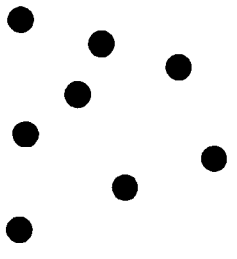


Figure 7.6
An example of dot counting stimuli

Test 6 Position Discrimination (20)

Each test stimulus consists of two adjacent horizontal squares, one with a black dot (5mm) printed exactly in the centre and one with a black dot just "off" centre (figure 7.7). In each of the 20 stimuli the "off" centre dot is in a different position within the square, in ten stimuli the centre dot is in the left square and in ten in the right square. The subject's task is to point to the dot that was in the centre. The number of correct choices is recorded.

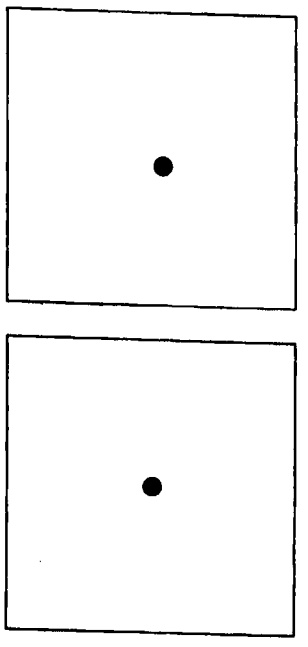


Figure 7.7
An example of Position Discrimination test

Test 7 Number Location (10)

These stimuli consist of two squares (62mm x 62mm), one above the other with a small gap between them (figure 7.8). The top square contains randomly placed numbers (1-9) and the bottom square contains a single black dot corresponding to the position of one of the numbers. The position of the dot is different in each of the stimulus cards and there are four different number arrays. The subject's task is to identify the number that corresponds with the position of the dot.

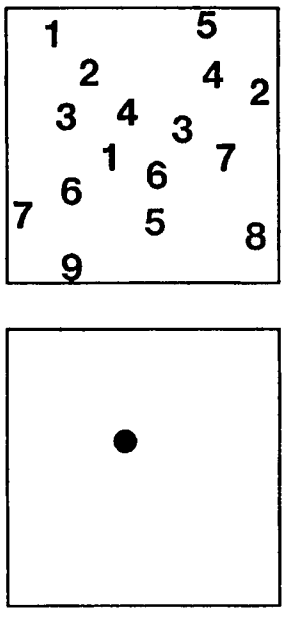


Figure 7.8
An example of Number Location test

Test 8 Cube Analysis (10)

The test stimuli consist of black outline representations of a three dimensional arrangement of square bricks (see figure 7.9). The two practice items are representations of three bricks. The ten test stimuli are graded in difficulty by increasing the number of bricks from five to 12 and by inclusion of hidden blocks. The subject is asked to report the total number of solid bricks that are represented in the drawing.

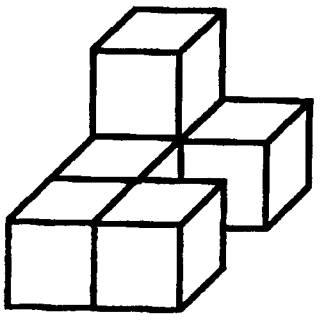


Figure 7.9
An example of Cube Analysis stimuli

7.5.5 Recognition Memory Test: *(Warrington, 1984)*

In this test, recognition memory was tested separately for faces and words. Fifty faces were shown at the rate of one every three seconds and subjects were asked to make a "pleasant" or "unpleasant" decision. Recognition memory was then tested by presenting each of the faces paired with a distractor. The subject was asked to choose which face they had seen before. A similar procedure was used with fifty words.

7.5.6 Verbal fluency test (FAS) *(Benton, Hamsher, Varney & Spreen, 1978)*

Subjects were required to verbalise as many words as possible in a 1 minute period beginning with a given letter of the alphabet. Three trials were performed, with the different letters F, A and S. They were instructed to omit proper nouns and words obtained by altering the prefix or suffix of an earlier response, and not to repeat the same word. The score was the total number of correct responses over the 3 trials.

7.5.7 Structured Imagery questionnaires *(see appendix B3)*

Lists of questions were compiled to investigate imagery ability. The questions required simple one-word answers and were designed to test imagery ability over a range of objects. The questionnaire consisted of 10 questions, each of which was read aloud to the subject. The questionnaires asked questions on shapes, letters, mental hue comparison and semantic decisions.

7.5.8 Vividness of visual imagery questionnaire (VVIQ) (Marks, 1973) (see appendix C4)

This questionnaire contains 16 items to be rated in terms of their evoked visual imagery along a 5-point rating scale. The items themselves are four familiar objects or scenes, each of which is to be rated on four particular aspects (see appendix C4). The respondents were assigned mean scores based on their responses across all 16 items. According to Mark's original specification, the VVIQ should be completed twice, first with the eyes open and then again with the eyes closed. Some researchers administer the VVIQ with no instructions while other simply give no indication in their published reports as to whether they have followed Mark's original procedure in this regard. In this study no explicit instructions were given as to whether the subjects' eyes need be

open or closed as previous research indicates there is no systematic difference between the two conditions (Issac & Marks, 1994; McKelvie, 1995)

7.6 Testing Conditions

Testing sessions never lasted longer than two hours to avoid subjects becoming fatigued and sessions were usually at least one week apart. Subjects were tested in their own home, in the room they most commonly used and felt most comfortable in. Appointments were always made to suit both the subject's timetable and preference. This was important with patients, as the time of day at which testing occurs could have a significant effect on performance and patients appear to be accurate at judging the time at which their condition is best.

7.7 Source Monitoring and Recognition Tests

7.7.1 Design

This study addresses whether relative to non-hallucinating PD patients and normal controls, hallucinating PD patients have more impaired source memory and confuse perceived and imagined memories. All groups saw and imagined seeing line drawings of common objects (e.g dog, table, tree). To encourage participants to focus on the items and their appearance, they were asked to rate how long it would take to draw the picture they were looking at or imagining (see Durso & Johnson, 1980). Later, participants were given a surprise memory test in which they indicated whether each item had been seen (picture), imagined (word) or was new, after which they were asked about their subjective judgements using the RCA paradigm. The conditions were as follows:

1. Picture at encoding, picture at retrieval. (per-per).
2. Picture at encoding, word at retrieval (per-img).
3. Word at encoding, picture at retrieval (img-per).
4. Word at encoding, word at retrieval (img-img)

7.7.2 Materials

The stimuli for the source monitoring experiment consisted of two packs of 120mm x 80mm cards with one stimulus on each card. The encoding pack consisted of 24 words for the imagery trials and 24 pictures for the perceived trials. The testing pack consisted of the same picture / word distribution, with 12 pictures and 12 words reinstated in the same format, the others were presented in the alternate form, thus producing the 4 experimental conditions. In addition, 24 distractors were added to the test pack, half of each format. In order to avoid a list effect, the allocation of items to picture or word format at encoding was counterbalanced.

The items used for the experiment were selected from Snodgrass & Vanderwart's (1980) set of standardised pictures. All the items were easily identifiable objects that could be described with a single noun. The drawings were all simple line drawings in black and white.

7.7.3 Procedure

The subjects were told that the experiment was to study how people make judgements about things that are seen or imagined. They were told that they would see a series of cards and they were to make a particular type of judgement for all the items. Participants were instructed that some of the cards would show a simple black-and-white line drawing, whereas other cards would give just the name of an object. They

were asked to imagine the item as a black-and-white line drawing and their task was to estimate how many seconds it would take to draw each picture or how many seconds it would take to draw each imagined item. Participants were explicitly told to create an image of each object for the imagery trials and to base their judgement solely on the image and not upon other information about the object such as its complexity or size. Participants were then given a brief practice session in which they were shown 4 cards and asked to make a drawing-estimation judgement for each. For the encoding phase of the actual experiment, 48 cards were presented for 5 s each, during which time participants stated aloud their judgement of drawing time while the experimenter recorded their responses.

After the card presentation, participants were interviewed on their experiences of Parkinson's disease. Fifteen minutes after the card presentation, they were given a memory test in which a series of 72 cards (24 words, 24 pictures and 12 word distractors and 12 picture distractors) were shown to them. They were to indicate whether each item had been seen as a percept (picture), or was imagined (a word), or was new, providing source scores. If they indicated that the item had been seen before, they were further asked to categorise each recognised item into those they 'remembered' (R) and those they 'knew' (K). It was explained that 'R' items brought to mind some kind of picture, image or association at the time of learning, and 'K' items were those which they definitely recognised but for which they had formed no particular image or association at the learning stage. An applicable example was given in each case. The test was self-paced, and the same random order was used for each subject.

7.8 Results

7.8.1 Neuropsychological

A one way ANOVA was performed on the scores obtained for each test considering the effect of group (hallucinator, non-hallucinator, normal controls). Where data were found not to be normally distributed (Kolmogorov-Smirnov test), an equivalent non-parametric Kruskal-Wallis one-way ANOVA was used. Table 7.2 summarises the results. Significant findings were further analysed *post hoc* using Tukey's test.

Overall Parkinson's patients were significantly impaired on the four tests of object recognition in the VOSP. In contrast, no significant impairments were observed on the four spatial perception tests (dot counting, position discrimination, number location and cube analysis). Hallucinators identified fewer object on both the incomplete letters task and the silhouettes task than the other two groups. On object decision the groups performed at a significantly different level, with the controls identifying on average more items (18.7), than the non-hallucinators (17.7), who identified more than the hallucinators (15.1). The same pattern of results was observed for the progressive silhouettes.

The two PD patients groups did not perform significantly differently from each other on the recognition memory test for words. The results for recognition memory for faces just reached significance with the hallucinators remembering fewer items (28.5) than the non-hallucinators (32.1). However, both PD groups performed significantly worse than the normal control group. The PD groups were also significantly more depressed than the control group, but were comparable with each other. There were no significant differences between groups on tests of imagery ability, vividness of imagery or verbal fluency.

Table 7.2

Comparison between normal control subjects, non-hallucinating and hallucinating subject for neuropsychological test measures

		Normals		Non-hallucinators		Hallucinators		F	
		Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*		
VOSP	*Incomplete letters(20)* ✣	19.30	0.66	19.25	0.79	17.47	1.00	29.00***	♣ ♥
	Silhouettes(30) ✣	19.72	3.80	19.30	2.03	17.65	4.90	7.26**	♣ ♥
	Object decision(20) ✣	18.70	0.87	17.75	1.07	15.18	1.32	52.64***	♣ ♦ ♥
	Progressive silhouettes(20) ✣	12.45	2.01	16.45	1.67	18.06	1.35	53.61***	♣ ♦ ♥
	Dot counting(10) ✣	9.50	0.69	9.40	0.68	9.06	0.75	1.94	
	Position discrimination(20) ✣	19.85	0.37	19.50	0.69	19.53	0.52	2.53	
	Number location(10) ✣	9.50	0.69	9.25	0.72	9.29	0.77	0.67	
	Cube analysis(10) ✣	9.50	0.61	9.25	0.64	9.36	0.61	0.83	
Recognition	*Words(50)*	39.50	4.86	31.45	6.74	29.24	5.51	16.72***	♦ ♥
	Faces(50) ✣	40.05	3.52	32.15	5.37	28.53	4.61	31.42***	♣ ♦ ♥
Imagery	*Shapes (10)* ✣	9.55	0.61	9.75	0.44	9.70	0.47	0.83	
	Letters (10) ✣	9.75	0.44	9.76	0.46	9.77	0.42	0.01	
	Living visual (10). ✣	9.65	0.49	9.70	0.47	9.76	0.56	0.24	
	Living non visual (10) ✣	9.70	0.57	9.75	0.44	9.88	0.33	0.74	
	Non-living visual (10) ✣	9.67	0.48	9.70	0.57	9.65	0.49	0.06	
	Non-living non-visual (10) ✣	9.70	0.47	9.63	0.48	9.82	0.39	0.45	
VVIQ (80)		38.65	7.53	35.25	10.90	32.35	6.29	2.49	
FAS		44.90	7.48	39.30	9.69	39.59	10.49	2.28	
BDI ✣		8.90	2.59	16.60	5.39	18.24	4.54	25.40***	♦ ♥

**p<0.01; ***p<0.001

✣ Data violated normality assumption

♣ Significant difference between hallucinator group and non-hallucinator group

♦ Significant difference between non-hallucinator group and control group

♥ Significant difference between hallucinator group and control group

In summary, the analysis of the neuropsychological data revealed that the hallucinators were only impaired on five of the tasks (Object decision, Silhouettes, Incomplete letters, Object decision, Memory for faces). This finding may reflect impairment to a single cognitive process, or it might result from a more complex combination of deficits. This explanation was investigated by performing an inter-correlational analysis on all five tests. As the scores on these five tests were found not to be normally distributed (Kolmogorov-Smirnov test), all the correlations in this chapter used Spearman's Rho. The neuropsychological results revealed only one significant correlation between the silhouette test and the object decision test ($R = 0.53$, $p < 0.05$). This is not surprising, as in both tests the subject has to identify an object in the form of a silhouette. In consequence, only object decision was considered in further analysis.

7.8.2 Recognition and source monitoring experiment

All the measures obtained from this experiment (recognition and source scores) were analysed using a three-way mixed ANOVA which considered the effects of encoding form (pictures, words), retrieval form (pictures, words) and group (hallucinator, non-hallucinator, normal) (see table 7.3). This procedure was followed by a correlational analysis considering the relationship between the neuropsychological scores which were found to discriminate the hallucinators from the other two groups and performance on this experiment. These correlations (Spearman's Rho) were performed on the experimental group of hallucinating PD patients in the aim to identifying a pattern of impairment which would typify an hallucinating PD patient.

Recognition scores

Table 7.3
ANOVA analyses of Recognition and R & K scores

Variable	Mean Score	R's	K's	R Proportion
	F	*F*	*F*	*F*
Effect of Group	32.24***	81.98***	1.256	28.42***
Effect of Encoding	3.96	0.093	5.34**	2.46
Effect of Retrieval	14.17***	0.726	7.19**	2.02
Group x Encoding	2.33	0.426	2.96	1.64
Group x Retrieval	1.01	3.36*	1.02	2.06
Encoding x Retrieval	0.41	4.03*	5.76*	11.45***
Grp x Enc x Ret	1.49	1.216	0.910	1.763

*p<0.05; **p<0.01; ***p<0.001

There was a main effect of retrieval form on the number of items correctly recognised, which confirmed that subjects performed better when they were tested on pictures than on words [F(1,54)=14.17; p<0.001] (see figure 7.10). The only other significant finding revealed a main effect of group [F(2,54)=32.24; p<0.001], as the normals recognised on average more items than the non-hallucinators (8.78 against 7.68), who in turn had better recognition than the hallucinators (6.19).

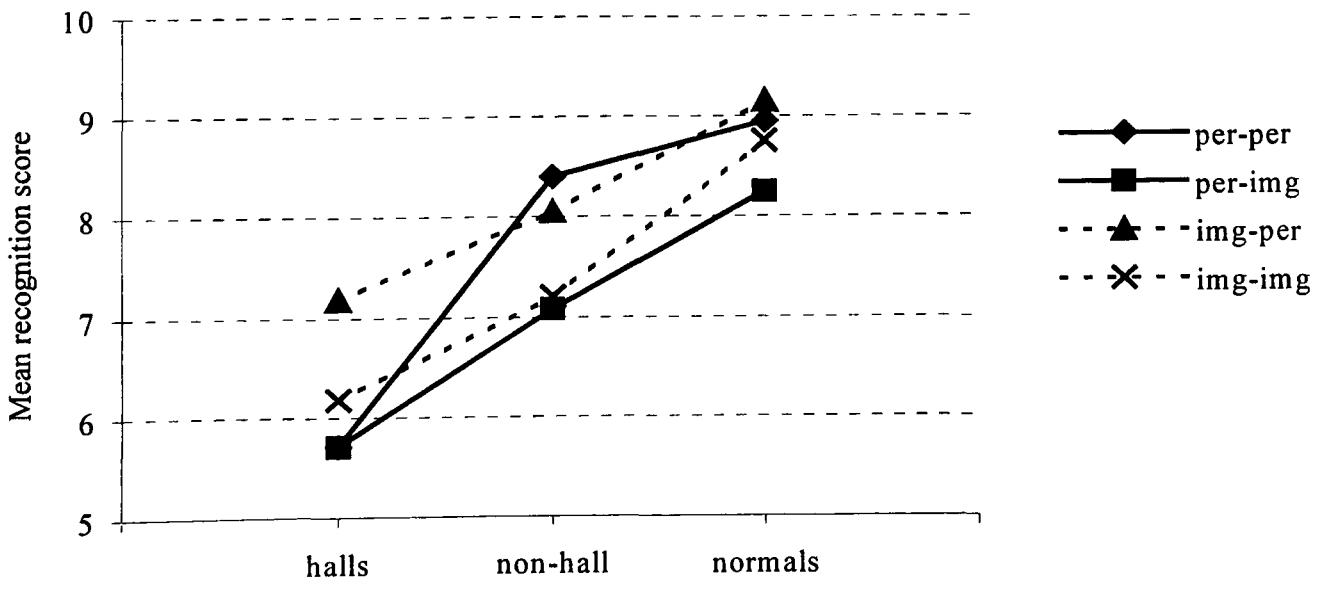


Figure 7.10
Mean recognition score in each condition of all three groups, showing how the encoding and retrieval affect performance. Maximum score in each condition was 12

The number of false alarms can be seen in table 7.4. Here the hallucinators produced significantly more false alarms than the non-hallucinators who in turn made significantly more errors the normal controls [$F(2,54)=7.69$; $p<0.01$]. However, to allow for the uneven number of distractors and target items, data were also analysed using two-high-threshold (THT) theory (Feenan & Snodgrass, 1990; Callaway et al., 1991; Brandt et al., 1992). The THT theory was used because of the independence of decision bias from discrimination. Its indices are easily computed from the hits and false alarm rates and were computed from the following formulae (Cowan, 1994):

Discrimination Bias (Pr) = (number of hits + 0.5 / number of targets+0.1) –

(number of false alarms + 0.5 / number of distractors + 1)

Response Bias (Br) = (number of false alarms + 0.5 /

number of distractors + 1) / (1 – Pr)

Results are represented in table 7.4. A one way ANOVA revealed that all groups were significantly different from each other [$F(2,54)=40.79$; $p<0.001$] on the measure of discrimination bias or memory efficiency (Pr). However, no significant differences were revealed between groups on response bias (Br). This indicates that the three groups had different memory abilities but this was not a reflection of a tendency of the hallucinators to make many false positives.

Table 7.4

Comparison between normal controls, non-hallucinators and hallucinators for recognition test measures (mean and standard deviation)

	Normal Controls (n=20)	Non-Hallucinators (n=20)	Hallucinators (n=17)	F (2,54)	*P* <
Correct recognitions	35.10 (SD 4.30)	30.95 (SD 3.38)	24.77 (SD 3.93)	32.64	0.001
False alarms	2.95 (SD 0.99)	3.40 (SD 1.56)	4.71 (SD 1.57)	14.99	0.01
Discrimination index Pr	0.60 (SD 0.10)	0.60 (SD 0.12)	0.32 (SD 0.11)	40.79	0.001
Response bias Br	0.35 (SD 0.11)	0.31 (SD 0.10)	0.31 (SD 0.11)	1.82	*n.s*

R and K responses

The analysis of the raw data (see table 7.3) showed that the number of correct R responses decreased significantly from 21.45 in the normal elderly controls to 17.35 in non-hallucinators and 9.59 in the hallucinator group [$F(2,54)=81.98$; $p<0.001$]. Although in the literature R and K data are frequently examined in raw form (Gardiner & Parkin, 1990: Mantyla, 1993), there are reasons why this may lead to inappropriate findings. As Rajaram (1993) points out, R and K responses always add up to the total recognition score, so therefore should not be treated as two levels of a factor in an ANOVA since they are not significantly independent. This is confirmed in this study as there was a significant correlation between R and K in all three groups. A more appropriate method has been proposed by Rajaram who suggests using the proportion of R responses to overall recognition responses (R+K) as a measurement.

A one way ANOVA can then be performed on these derived scores to investigate how the relationship between R and K changes across the groups (see table 7.3). Using such an analysis showed that patient groups did have a significant effect on the mean R/(R+K) ratio [$F(2,54)=28.43$; $p<0.001$]. Post hoc analysis revealed that the proportion of mean R responses was significantly lower in the hallucinators (see figure 7.11). The advantage of using this proportion measure is that it takes into account overall recognition performance which is particularly important given that this was shown to be significantly different across groups. The only other significant finding was an interaction between encoding and retrieval, but as it failed to interact with the variable of group, it is not discussed further.

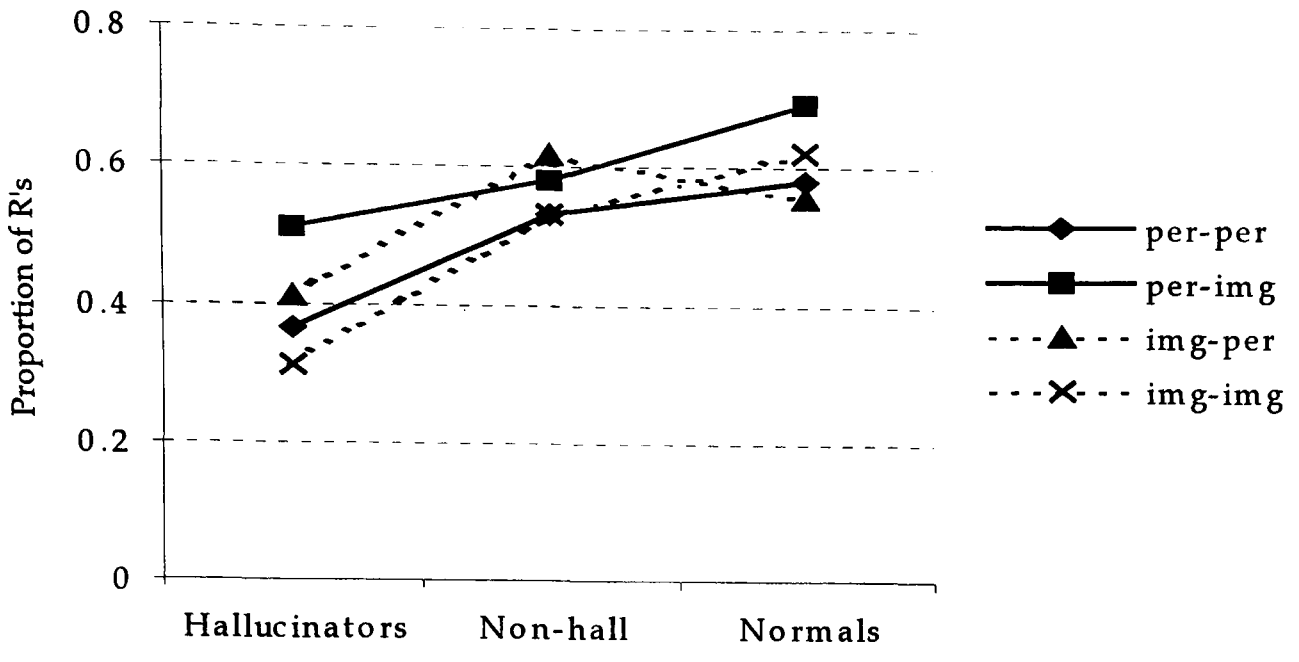


Figure 7.11
Mean proportion of R responses in each condition of all three groups

A correlational analysis with the hallucinating group revealed no association between raw recognition scores and the neuropsychological measures in the hallucinating group of PD patents. This suggests that overall recognition scores are independent of object recognition performance. Following the earlier discussion regarding R and K scores, only R proportions were considered in the correlational analysis performed on the hallucinating group data. This revealed two significant negative correlations. The first, between Rs in the imagery-percept condition and the incomplete letters task ($R = -0.54$, $p < 0.05$), and the second between the word-word condition and the object decision task ($R = -0.62$, $p < 0.01$). Interestingly, no significant correlations were found when the stimuli were encoded as pictures.

Source memory results

In addition to recognition performance, for each item they correctly recognised, subjects were asked to specify whether they thought they originally encoded the item as a percept (picture) or as an image (word). A 3 way group x encoding x retrieval ANOVA was performed on the raw number of items correctly allocated to their source (see table 7.5).

Table 7.5
ANOVA analyses of Source Scores

Variable	Mean Score	Source Proportion
	F	*F*
Effect of Group	105.17***	26.37***
Effect of Encoding	0.34	2.90
Effect of Retrieval	20.07***	0.01
Group x Encoding	0.03	2.59
Group x Retrieval	3.36*	0.79
Encoding x Retrieval	16.00***	10.90***
Grp x Enc x Ret	3.68*	3.22*

*p<0.05; **p<0.01; ***p<0.001

The analysis revealed a main effect of retrieval [$F(2,54)=20.07$; $p<0.001$] since testing with pictures led to better source allocation than testing with words (5.78 against 5.04 respectively). A main effect of group [$F(2,54)=105.17$; $p<0.001$] and post-hoc follow up suggested that the three groups performed differently from each other ($p < 0.05$). The normal group allocated most items to their correct source (6.66), followed by the non-hallucinating Parkinson's patients (5.80) while the hallucinators performed worst (3.77) (see figure 7.12).

The two variables producing main effects were also found to interact, suggesting the greatest effect of the retrieval condition was in the non-hallucinating PD patients,

followed by the hallucinators, and little effect on the normal controls (see figure 7.12). The interaction between encoding and retrieval [F(1,54)=16.00; p=0.001] suggests that when subjects encoded a word, their source judgement remained similar across retrieval conditions. In contrast, source judgement of encoded pictures was much better when tested on the original picture than on a word. This suggests that the source judgement of encoded percepts is more dependent on test form than words. The data analysis also revealed a significant three way interaction [F(2,54)=3.68; p=0.032], as the interaction between encoding and retrieval was greatest in the non-hallucinating PD patients, less in the hallucinators and least in the normal controls.

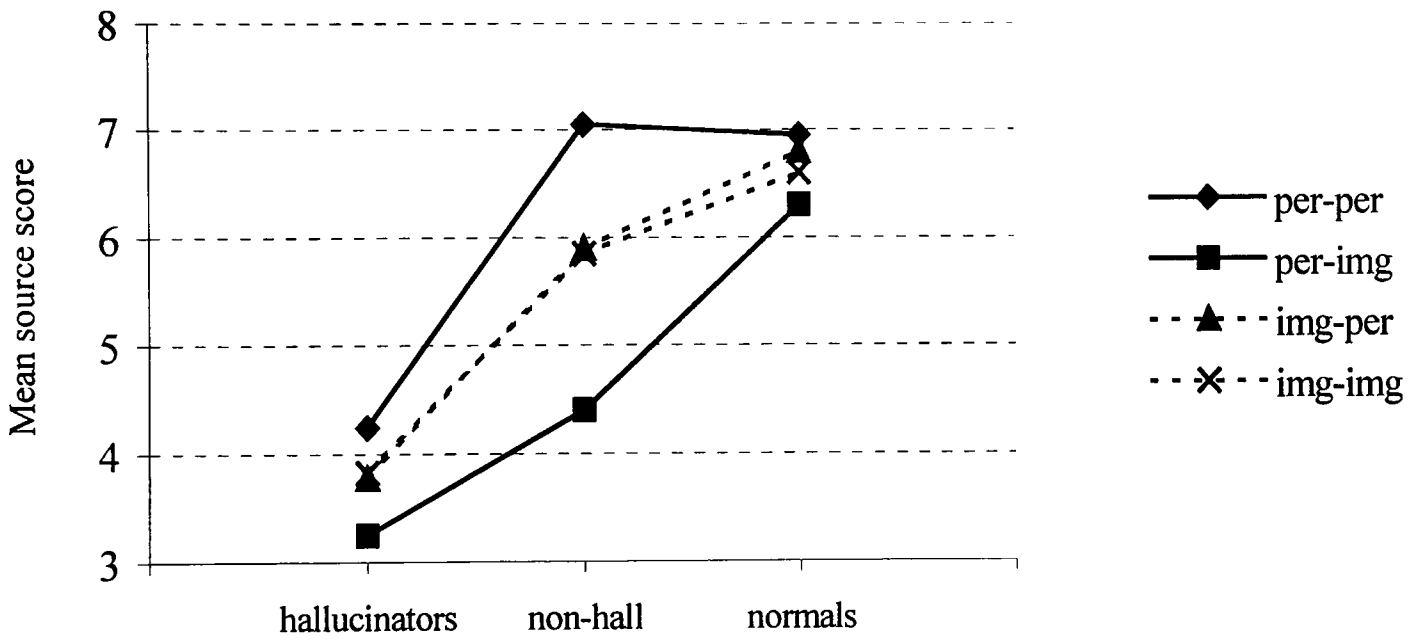


Figure 7.12
Number of recognised items correctly assigned to initial presentation modality for each group

Source score proportions

As the number of items correctly allocated to source is dependent on the recognition score, raw source memory scores were transformed into a proportion of the total recognition scores using the following formula:

Number of items assigned to correct source / total recognition score.

The resultant transformation we termed *source proportions.* A 3 way ANOVA on these source proportion data (table 7.5) revealed only one main effect, that of group [$F(2,54)=26.36;p<0.001$], which a post-hoc test confirmed was the result of the normals being better at judging source than either of the patient groups : 0.809 against 0.769 and 0.610 for the non-hallucinators and hallucinators respectively (see figure 7.13).

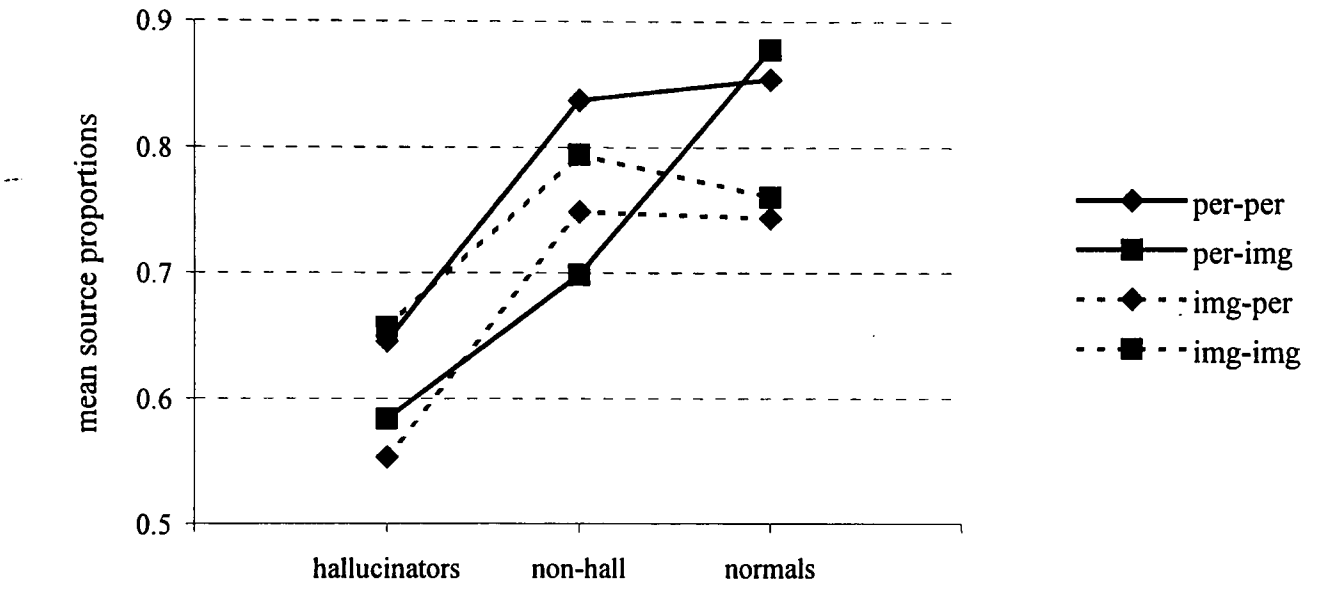


Figure 7.13
Mean source score proportions across each condition for each group

The analysis revealed two further interactions. A significant 2 way interaction [$F(1,54)=10.91$; $p=0.002$] between encoding and retrieval appeared to confirm the well established retrieval specificity effect (Tulving, 1983). In this instance, items sources were best identified when they were presented in the same form as they had been encoded, as can be seen in figure 7.14.

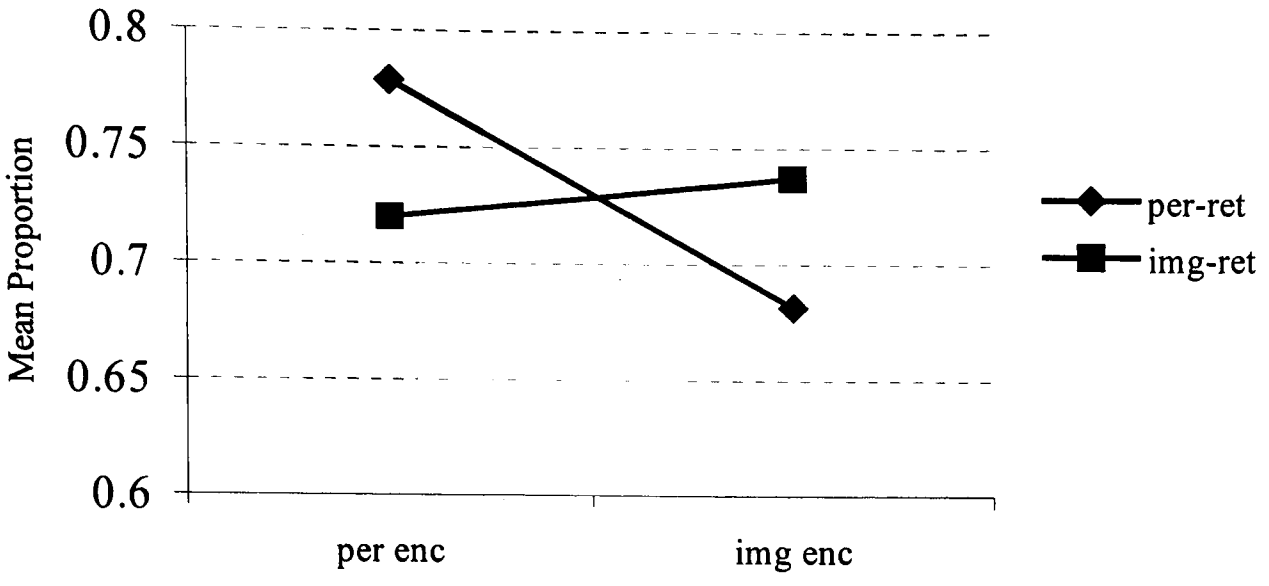


Figure 7.14
Mean source score proportions for encoding (enc) and retrieval (ret) for all groups

In addition, these data suggest that when an item was retrieved as an image, subjects were as accurate at judging its source whether it was encoded as a word or a picture. In contrast, when the item was retrieved as a picture, source was more accurate when it had been encoded as a picture than as a word. This suggests that retrieval specificity was more important when making source judgements on pictures than on words.

Of more interest was the three way interaction involving group x encoding x retrieval [$F(2,54)=3.22$; $p=0.048$]. In order to clarify this interaction, 2 way ANOVAs considering encoding form (percept, image) against retrieval form (percept, image) were performed for each subject group. The results of these analyses for the hallucinating PD group [$F(1,16)=4.69$; $p=0.46$], and the non-hallucinating PD group [$F(1,19)=8.41$; $p=0.01$] can be seen in figures 7.15 and 7.16,

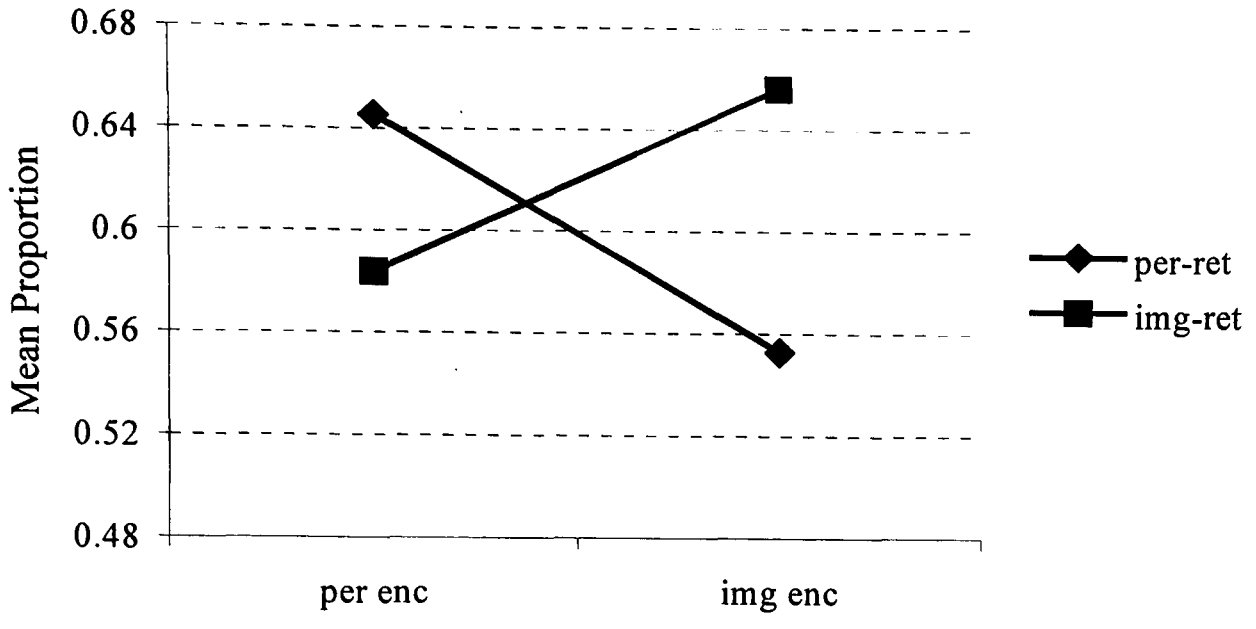


Figure 7.15
Mean source score proportions of encoding and retrieval for PD hallucinators

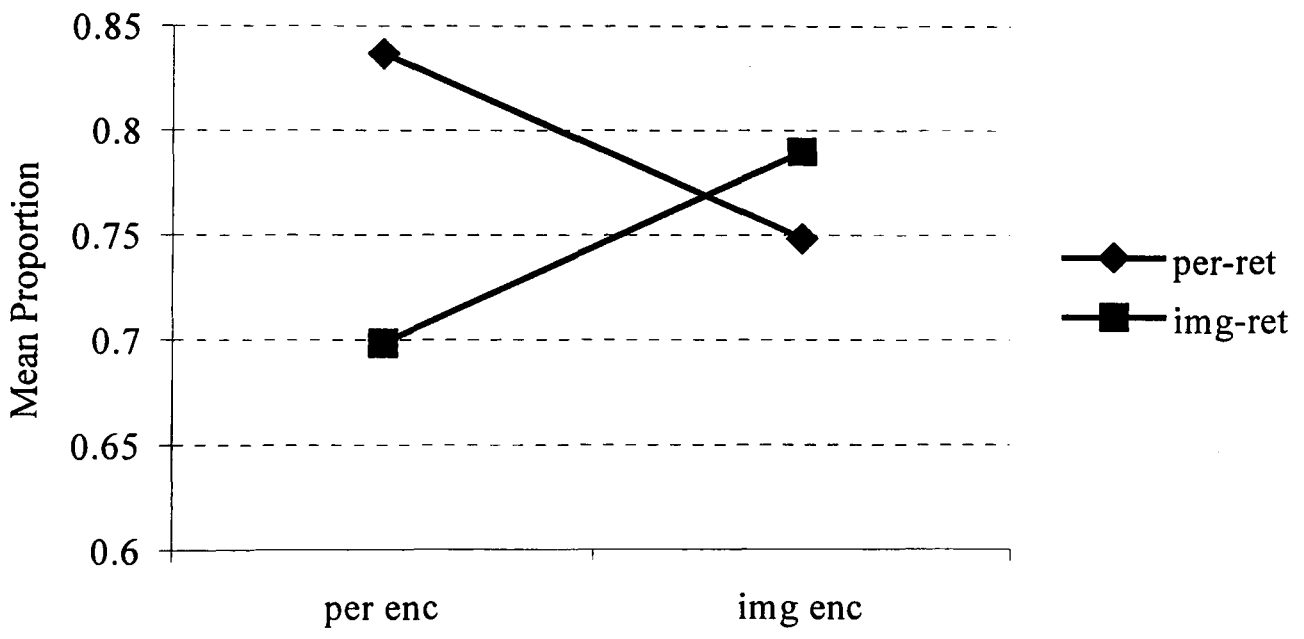


Figure 7.16
Mean source score proportions of encoding and retrieval for PD non-hallucinators

In both these groups, there was clear effect of retrieval specificity, as their source allocation was best when test and encoding forms were the same. In contrast, normal

subjects performed better when encoding pictures, regardless of retrieval form (figure 7.17).

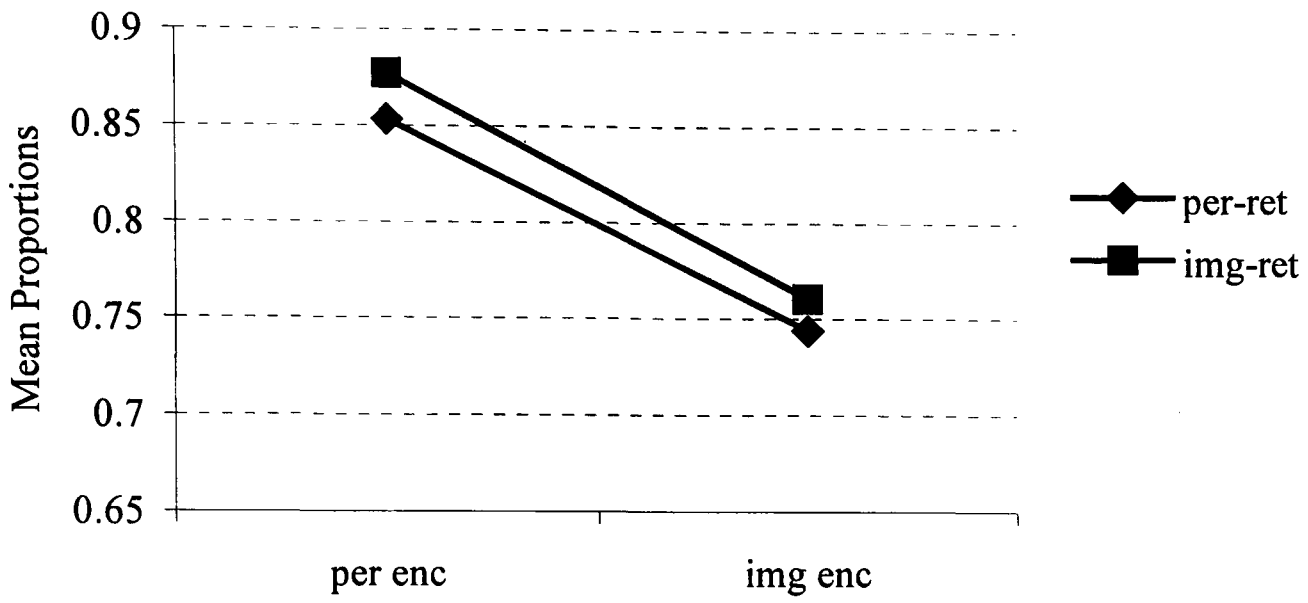


Figure 7.17
Mean source score proportions of encoding and retrieval for normal control group

Furthermore, while this interaction was the only significant effect found in either of the patient groups, in the normal group the only significant finding was an effect of encoding, which again can be seen as being caused by higher scores when the items were encoded as pictures [$F(1,16)=10.35$; $p=0.005$].

The findings so far suggest that the two patient groups are in fact comparable. This was tested in a further ANOVA considering these two groups. When the two Parkinson's groups were compared to each other, the only main effect was between the groups [$F(1,35)=24.72$; $p=0.001$], which revealed that the non-hallucinators were better at judging the source of an item than the non-hallucinators. There was also a

two way interaction between encoding and retrieval form suggesting that overall, PD subjects had difficulty in "switching" between different encoding and retrieval forms [F(1,35)=12.610;p=0.001] (figure 7.18).

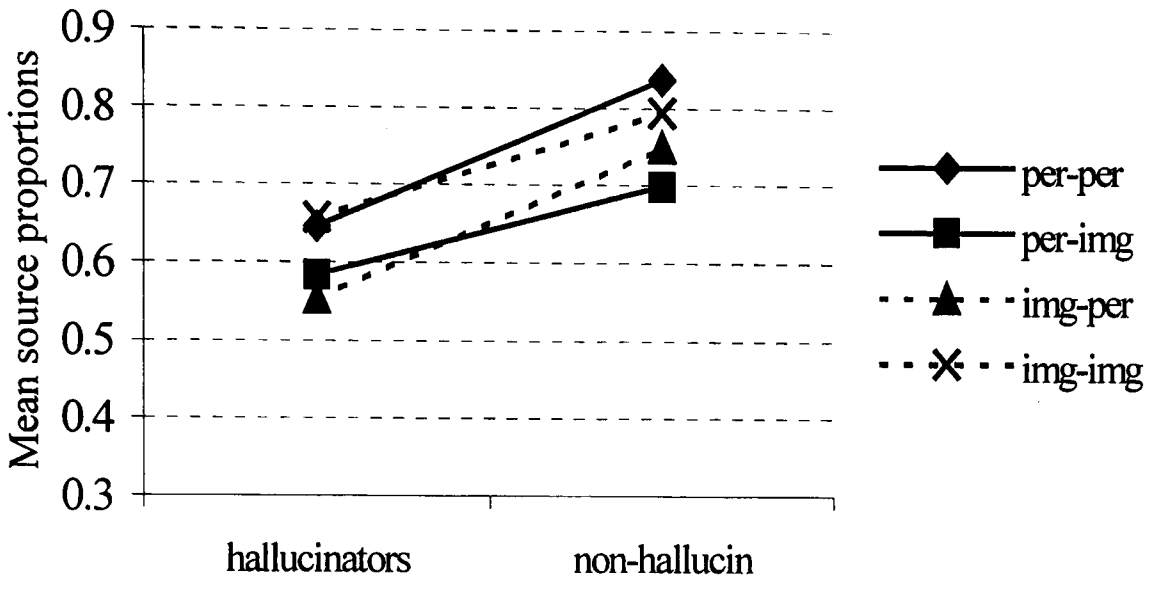


Figure 7.18

Mean source score proportions of encoding and retrieval for Parkinson's groups

There was, however, no interaction involving group, supporting the idea that the variables of encoding and retrieval format affected both groups similarly. When the normal control group was compared with each of the patient groups in turn, a somewhat more complex pattern of relationships was revealed.

When the hallucinators were compared with the control group, there was a main effect of group [F(1,35)=49.56; p=0.001], which indicated that the control group was better at judging source that the hallucinators, and a main effect of encoding [F(1,35)=3.98; p=0.50], which was due to subjects recognising more items when encoded as pictures. The encoding x retrieval and group x encoding x retrieval interactions were also found

to be significant, [F(1,35)=3.79 p=0.059, and [F(1,35)=4.50; p=0.41] respectively (see figure 7.19).

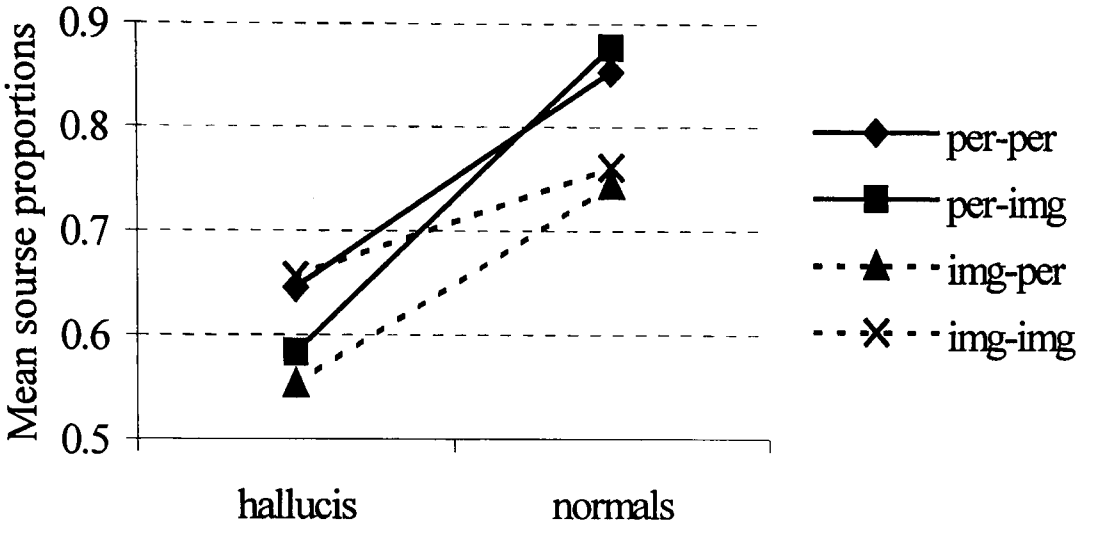


Figure 7.19
Mean source score proportions of encoding and retrieval for hallucinators and normal control group

When the non-hallucinating Parkinson's patients were compared with the normal group, there was no main effect of group. There were two significant interactions involving group with encoding in a 2-way relationship [F(1,38)=5.46; p=0.023] and with both encoding and retrieval in a 3-way interaction [F(1,38)=6.70; p=0.014]. The 2-way interaction with encoding suggests that the non- hallucinating Parkinson's patients allocate source equivalently well whether they encode a word or a picture; in contrast, the normals perform better when they encode a picture (figure 7.20)

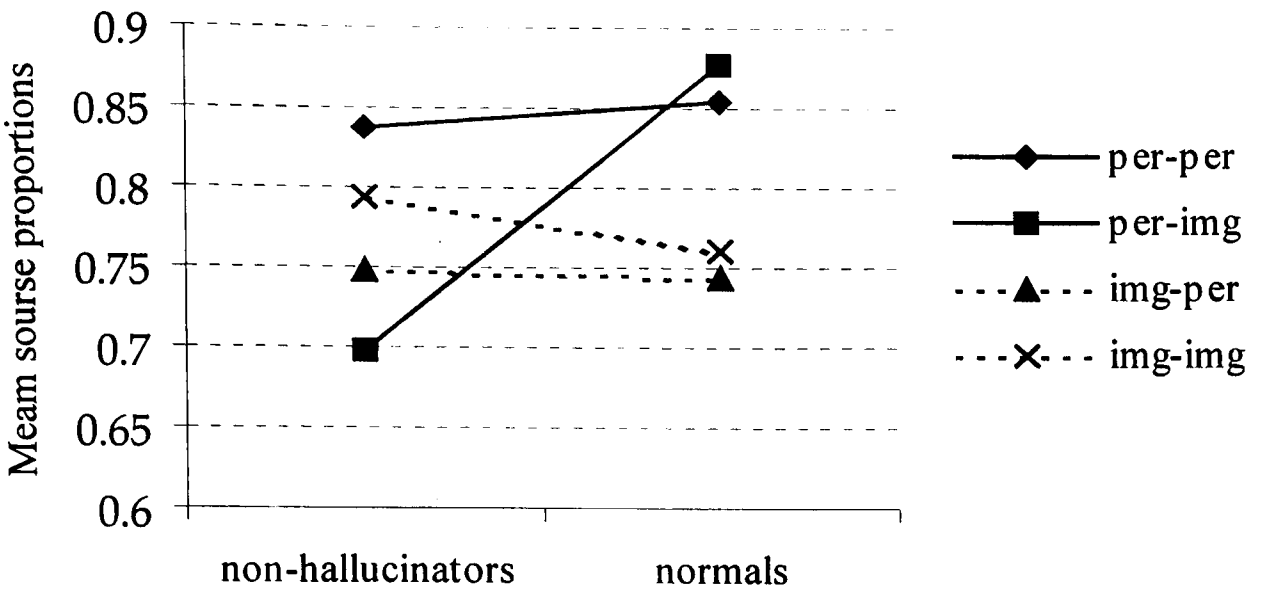


Figure 7.20
Mean source score proportions of encoding and retrieval for non-hallucinators and normal control group

This dissociation between the non-hallucinator and control groups emanates from only one condition, where items are encoded as percepts and retrieved as images. In this condition, the non-hallucinating Parkinson's patients perform worse than in other conditions than the control group. In the other conditions non-hallucinators' performance is better than or comparable with controls (see figure 7.20). Normal controls are better at judging source when they encoded a picture than when they encoded a word. Unlike the non-hallucinating PD patients, the hallucinating patients' performance was impaired on both the "cross modal" conditions: they performed best when there was full stimulus reinstatement than when the encoding and retrieval forms were different, but both impaired compared to the controls (see figure 7.19). This can be seen clearly if the retrieval and encoding forms are collapsed to the one variable of retrieval specificity, with two levels, "same" and "different" as shown in figure 7.21 below.

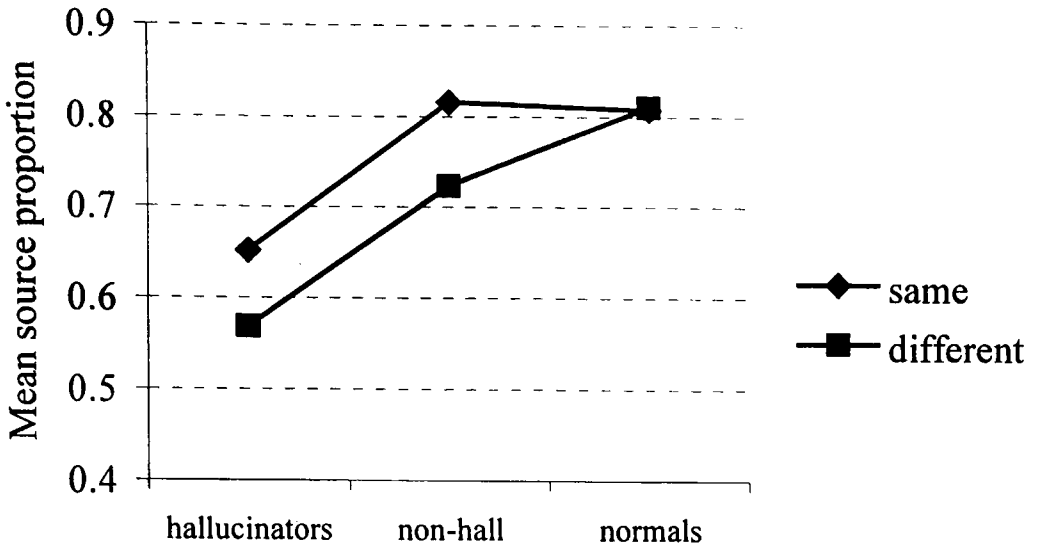


Figure 7.21
Mean source score proportions of retrieval specificity for all groups

In the hallucinating group, correlational analysis of source proportions and neuropsychological measures revealed two significant correlations between the precept-imagery condition and the incomplete letters task ($R = -0.56$, $p < 0.05$) and between the imagery-imagery condition and the progressive silhouette task ($R = -0.48$, $p<0.05$). These results were mirrored in the raw source scores.

7.9 Summary of Results

In summary, the results of the neuropsychological tests showed that hallucinators were significantly impaired on tests of object decision and progressive silhouettes. This group also remembered significantly fewer faces in the Warrington recognition memory test. The source monitoring experiment revealed that the hallucinating group was the most significantly impaired of the three groups on recognition of previous encoded stimuli, but was disproportionately poor at remembering the source of an item. They also relied on the "feeling of knowing " or K responses to make their judgements. The most striking difference between the non-hallucinators and the hallucinators was that the hallucinating PD patients had impaired source judgement

whether the encoding stimuli were fully reinstated at retrieval or not In contrast, the non-hallucinating PD group were only impaired when this reinstatement was absent, performing at normal levels when reinstatement occurred.

In the hallucinating group, significant correlations were found only between object recognition tasks from the VOSP and performance on the recognition conditions where the stimuli were encoded as images.

7.10 Discussion

Hallucinations are an important symptom of Parkinson's disease because they may seem bizarre and frightening to patients and their caregivers, and because their presence often has diagnostic, and treatment implications. This study focused on neuropsychological performance, recognition memory and source monitoring in hallucinating patients, non-hallucinating patients and an age-matched control group.

When discussing neuropsychological measures in PD, a clear separation must be made between impairment on visual tasks, and cognitive impairment. The PD group did not show any impairment of a degree that pointed to a demented state using estimates of IQ or the MMSE. The current rates of dementia in PD range from approximately 10% to 20% (Girotti et al., 1988; Mayeux et al., 1988; Tison et al., 1995). The MMSE scores were lower in the PD group compared with normal, however, all subjects scored above the cut-off of 24 points. Also, since all the patients volunteered for the study and in some cases booked their own appointments for testing times, this research may well have been biased in favour of those patients with PD who had the least cognitive impairment.

The Beck depression inventory (BDI) indicated that patients with PD were comparable to each other on the depressive scale but were significantly more depressed than controls. However, it must be kept in mind that some of the items on the scale may not necessarily signify depression but rather reflect symptoms of PD, particularly motor impairment. Item-by-item analyses of test responses, however, suggest that a certain amount of true affect change does occur. Considering the impact of PD in terms of mortality, some depression of mood is not surprising.

Research on the impact of PD on verbal fluency has produced a wide variety of findings. Although Dubois et al. (1988) observed a significant impairment in PD performance on letter fluency tasks, their PD patients also showed signs of general intellectual impairment. Gurd and Ward (1989) observed a deficit in PD performance for both letter and semantic fluency tasks but they did not provide information about the patients' mental status. It is possible that some or all patients were demented. Thus, in both studies the observed fluency deficit may have been due to general cognitive impairment that is not universal in PD (see Hanley et al., 1990). As already stated, scores on the MMSE in this study were within the range to assume normal cognitive functioning for all groups. Furthermore, if verbal fluency is highly sensitive to mental status, as it is reputed to be (Appell et al., 1982; Martin & Fedio, 1983) there should be no significant performance differences between non-demented PD patients and age-matched control. The results in this study support this assertion.

The neuropsychological results indicated that the PD patients with hallucinations performed poorly on tests of object recognition and had significantly impaired recognition memory of faces compared with the other groups. However, no

differences were found on tests of spatial ability between groups. This is at first sight may appear a little surprising since many have considered the proposal that patients with PD had a generalised visuospatial deficit (Boller et al., 1984). Since then a number of studies have challenged this idea. Brown & Marsden, (1986) failed to find a deficit on a test of left-right discrimination and "mental rotation" and Taylor et al. (1986) found no significant differences on visuoperceptual and visuospatial tests in terms of accuracy. Other studies have also revealed similar results (Ransmayr et al., 1987). In our sample, these findings were upheld, with the PD groups performing as well as the normal controls.

On the VOSP, the hallucinating PD patients were found to be impaired on the tests of object recognition but not on any of the spatial tests. Interestingly, all the object recognition tasks involve the identification of silhouettes of common objects and animals. This lack of fine detail inherent in the stimuli may have lead to the mis-identification of objects. Our impression is that hallucinators were reasonably quick in their choice of silhouette in the object decision tasks, however their confidence was not justified by their scores. The hallucinators seemed to have a "visual silhouette agnosia". When considered in conjunction with the significant correlation found between the correct identification of objects in the object decision task and the recollective judgement of familiarity and between correct source allocation in the imagery-imagery condition of the source task and performance on the progressive silhouette task, this seems to suggest that the hallucinating subjects rely on familiarity and automatic processing to identify objects correctly. Correct identification of objects in these tasks required "top down" processing, an activity that may be involved in the hallucinatory experience.

A quite reasonable and satisfactory account of simple hallucinations is that they are caused by the discharge of peripheral retinal cells, as well as the firing of cells in low-level visual processing areas such as V1. Indeed, ophthalmology texts detail a number of peripheral eye conditions including glaucoma, impending retinal detachment, traction of the vitreous on the retina, or retinal microembolism that may give rise to simple flashes of light (Roy, 1993). However, the attempt to explain PD hallucinations by direct application of this idea is clearly insufficient for the simple reason that hallucinations in PD are usually highly formed, indicating that higher-visual areas are certainly also involved, especially those contributing to the processing of object characteristics such as shape, motion and colour (see chapters 3-5). Hallucinating patients may not only have the deficits in low level vision which seem to accompany PD (Harris, 1998), but also have a functional lack of visual input to the brain. In the narrower sense, the term "sensory deprivation" is used to mean the disruption of normal sensory functioning, so that central neural processing is deprived of information from the environment regardless of the content of that environmental information. The disruption can occur in peripheral processing areas, including the retina, optic nerves or optic tract. However, the broad definition of "sensory deprivation" could include the information available to an intact sensory system from an ill-defined object or ambiguous environment. Although all the subjects had adequate eyesight to read script of size N10 presented on reading charts and showed no signs of visual disturbances, hallucinating PD patients in this study seemed unable to extract information from impoverished stimuli, as in the silhouette, or the environment, as in dim surroundings. This absent or random information in the visual system may trigger more complex and patterned activity in higher-level visual areas

forming the start of the hallucinatory process. However, the question which still remains, is why this misinterpreted information is then projected into external space.

Sietz and Malholm (1947) proposed that hallucinations might be the result of abnormally vivid imagery, a theory developed by Mintz and Alpert (1972), who argued that defective reality monitoring was also required for hallucinations to occur. In this study the hallucinating patients had a slightly higher imagery ability as assessed by the VVIQ scores than the other two group, however, this difference was not significant. The hallucinators had intact imagery while having poor object recognition. Moreover, their ability to interpret the source of a stimuli was significantly impaired when compared with the non-hallucinator and normal controls.

In previous studies using auditory tasks, hallucinators displayed a liberal response bias (Br), which indicates the propensity to accept a stimulus as a target in cases of uncertainty as to whether the stimuli is old or new, rather than to any perceptual disorder. In the current study, no significant differences in response bias were found between the three groups, with hallucinators being no more liberal than controls. Furthermore, the results of both Bentall and Slade (1985) and Rankin and O'Carrol (1995) suggested that hallucinations were not related to a perceptual deficit. The current results however, show that hallucinations are related to a measure of memory accuracy in recognition. Hallucinators had significantly lower discrimination index (Pr) scores than the other two groups. This indicates that hallucinations in PD are associated with sketchiness of traces of real events.

The aim of this study was also to address whether hallucinators are more susceptible to source errors between imagined and perceived event than non-hallucinators and controls. Although hallucinators were poor at the recognition component of the experiment they performed disproportionately worse at the source memory tasks. Poor recognition alone provides an unlikely account for such a large source deficit because the performance of old-new recognition and source monitoring were differentially affected by the item's source: recognition was higher for imagined than perceived items, yet source monitoring produced similar scores for perceived and imaged items. The pattern of performance in PD subjects suggests that the greatest confusion is not with imagery or perception per se, but with "switching" between internally and external generated stimuli.

Although the performance of hallucinators and non-hallucinators gave a similar pattern of results, non-hallucinators had comparable performance to controls on imagery encoding tasks. Hallucinations appeared to be associated with a greater propensity to report imaged stimuli as percepts. This suggests that patients with hallucinations believe that the mental image triggered by a word at acquisition phase was a real picture. Memory performance was improved when the encoding form was fully reinstated at retrieval, i.e. when retrieval and encoding were in the same form.

There are two interpretations for an increased response bias towards picture misattributions: the first is that patients with hallucinations have particularly rich imagery: either they are more prone than the other patients and normal controls to make a mental image from a word stimulus, or the mental image they make is more vivid. Thus, the mental image would be more likely to be mistaken for a real percept

(Johnson, 1991). The second interpretation is that hallucinators have a deficit in the ability to compare imaginary and real events. Therefore, the mental images would not necessarily be more vivid than in normals, but these patients would have a lax criterion in terms of giving them the internal/external status of actual events. In this study, the imagery ability, as measured by the VVIQ and the structured imagery questionnaires, was comparable to normals in both PD groups. Therefore, it seems that hallucinations are associated with a lax criterion to accept an imaginary event for a real one. The results from this study are in agreement with the theory that hallucinations are associated with a reality monitoring deficit (Frith, 1992). They are also compatible with Bentall and Slade (1985), Rankin and O'Carroll (1995) and Brebion et al., (1998), which show that hallucinations are associated with an increased propensity towards erroneous detection of events which had not occurred.

There are ongoing debates about the nature of implicit and explicit memory and whether these are the best terms to use (Hirst 1989). Despite the various theoretical interpretations and different uses of the terms implicit and explicit, there seems to be a general agreement about the "key feature" of implicit memory, that is, it occurs in the absence of a conscious recollection of the episode (Wippich, 1992). Explicit measures such as free recall require conscious awareness of the learning episode, whereas performance found on implicit tests do not. This distinction has been addressed in this study by the recognition and conscious awareness (RCA) paradigm. Hallucinators relied on a "feeling of knowing" to identify the items presented. This indicates that although the items appeared familiar to the hallucinating patient, the patient can remember little of what they experienced at the time the item was seen or imaged. In other words a K response was made to the items when the subject could not

consciously recollect its previous occurrence. It has been argued that reality is not given directly in perceptual and memory representations but is the product of judgement processes (Johnson, 1988; Johnson & Raye, 1981). Reality testing of ongoing perception and reality monitoring of memories are complex judgement processes that are subject to error and more difficult in some situations that others. Hallucinators seem to have limited abilities to encode either stimuli or context, which produces impoverished memories or judgement processes, which in turn leads to errors in source monitoring and "remembering" the event.

7.11 Conclusions

Non-threatening visual hallucinations are the commonest perceptual misinterpretation seen in treated PD (Moskovitz, 1978) and as such, this clinical phenomenon is of interest and has a relevance to PD treatment. This study shows that compared to non-hallucinating PD patients and age-matched controls, hallucinating PD patients have difficulty in identifying impoverished or degraded objects. They are also less adept at judging whether an item has been imagined or perceived, and problems on "recalling" the recollective experience of the encoding event.

Hallucinations in mobile periods due to L-Dopa therapy could be due to over stimulation of the mesolimbisc and mesocorticolimbic dopamine receptors. In this study, however, it is more difficult to explain the occurrence of hallucinations this way as patients were taking comparable doses of L-Dopa. Furthermore, some patients experienced the phenomenon during immobile periods.

In light of the finding of this study and the study in chapter 6, hallucinations in PD seem to be a complex interaction of visual disturbances, poor source monitoring and impoverished recollection. Source monitoring processes include not only the retrieval of information, but also the interpretation of what is received. Here, the characteristics of the mental experience are provided by the sensory detail embedded in the spatial and temporal context of the event. The propensity to project internal events onto external reality may be as a consequence of the over-reliance on previously stored schemas, which on occasion "fills in" for missing detail. This together with poor judgement on the relative contribution of "top down" or "bottom up" processes leads to modification of what is experienced.

In conclusion, this study has demonstrated that compared with matched control groups, PD patients who suffered from visual hallucinations in the past three months showed greater impairments in visuoperceptual and source monitoring processes, while retaining imagery ability. These factors were also combined with a greater reliance on the "feeling of knowing" of previous experience. It would therefore appear, that the hallucinatory experience may arise from a complex association of perceptual, imagery, memory, and metamemory factors.

Chapter 8: General Discussion

In this last section of the thesis, the major findings of the neuroimaging studies are summarised, explanations for the hallucinations are explored, and finally, future directions for research are offered.

At the beginning of this thesis, a review of the literature revealed that whilst the topic of visual imagery had been substantially researched the nature and location of the underlying neural mechanisms were not well understood. Today, visual neuroscientists still debate whether the cortical areas that subserve visual imagery are identical to those that underlie visual perception. One side maintains that visual imagery and visual perception are mediated be a common neural substrate that includes early visual areas (Goldenberg et al., 1989: Kossyn el al., 1993; Kosslyn et al., 1995; Le Bihan et al.,1993) and the other side argues that visual imagery does not involve early visual areas but rather high-level visual areas only (Behrmann et al., 1992; Charcot et al., 1992; Decety et al., 1992; D'Esposito et al., 1997).

There is little room to doubt that retina and occipital cortex are involved in vision, since, for example, a variety of lesions in these structures can produce blindness for the affected area of the visual field. The extent to which they are involved in internal imagery and if a misattribution of internal images can result to the experience of visual hallucinations is still a matter debate. Sietz and Malholm (1947) proposed that hallucinations might be the result of abnormally vivid mental imagery, a theory developed further by Mints and Alpert (1972), who argued that defective reality testing was also required for hallucinations to occur. Horrowitz (1975) proposed that

hallucinators might suffer from an imagery deficit, causing them to misattribute occasional vivid images to an external source.

The goal of section 1 of this thesis was to identify the functional roles played by different regions of the brain in "experiencing" visual stimuli of both external and internal sources. Comparison of these brain regions revealed functional processes underlying imagery and perception and possible sites of convergence between the two experiences.

Reports of hallucinations detailed in this thesis suggest that the images present, "move". In chapter 3 we examined the sub-modality of motion in vision and ask if the same neural substrates are utilised when mentally transforming an object through space as when seeing the object move in the "real world".

Functional MRI (fMRI) was used to investigate local changes in blood flow in the human visual cortex of healthy volunteers while performing perception of both rotational and linear motion and mental transformations of the same stimuli. In the perception of rotation task subjects viewed a pair of figures similar to those described by Shepard and Metzler (1971), one of which was rotating. In the mental rotation task subjects mentally rotated one of two stationary figures into the same orientation as the other and then decided whether the two figures were identical or mirror images. The control task was identical except both of the cube assemblies were stationary and in the same orientation. The linear motion experiment consisted of perceiving and imaging motion with no rotational component. Analysis of group data for perception of rotational and linear motion showed activation in areas corresponding to V5 as

defined in earlier studies. Both rotational and linear imagery activated Brodman Area (BA) 19 but did not activate V5. An area within the inferior temporal gyrus, representing an inferior satellite area of V5, was activated by both the rotational perception and imagery tasks, but showed no activation in response to linear motion, either perception or imagery. Some premotor activation was seen across all tasks. The findings demonstrated the extent to which neural substrates for imagery and perception overlapped and revealed functional specialisation within motion perception and imagery processing systems.

In chapter 4 we extended the work on imagery to examine similarities and differences between perceptual and imaginal networks within the single visual submodality of colour. Our results show that colour perception activates the posterior fusiform gyrus bilaterally (area V4), plus right-sided anterior fusiform and lingual gyri, striate cortex (area VI), and the left and right insula. Colour imagery activated right anterior fusiform gyrus, left insula, right hippocampus and parahippocampal gyrus, but not V4 or V1. The findings reconcile neurological case studies suggesting a double dissociation between deficits in colour imagery and perception and point to anterior fusiform, parahippocampal gyri and hippocampus as the location for stored representations of coloured objects. The functional anatomy of these perceptual and imaginal networks was centred on the region of the fusiform and lingual gyri and as such suggest a "processing stream" where imaginal and veridical colour is represented. In chapter 4 we investigated an illusional colour after-effect (The McCollough effect), which unlike imaginal colour was perceived as arising from the external world. The colour was "real" and "external" to the induced subjects but absent for other observers, an experience very akin to an hallucination. Two fMRI experiments were carried out

to investigate the cortical network activated when perceiving coloured grids, and experiencing the McCollough effect (ME) (McCollough, 1964). Our results showed that perception of red-black and green-black grids activate the right fusiform gyrus (area V4) plus the left and right lingual gyri, right striate cortex (V1) and left insula. The ME activated the left anterior fusiform gyrus as well as the ventrolateral pre-frontal cortex, and in common with colour perception, the left insula. This study not only confirmed the critical role of the fusiform gyrus in actual and illusory colour perception, but also revealed localised frontal cortical activation associated with the experience of illusory colour. This would suggest that a "top-down" mechanism is implicated in this illusion. The "filling" of the grids with colour emphasises the inherent capacity of the brain to generate, or construct, a meaningful experience without direct correspondence to sensory stimuli. A similar process may be occurring in hallucinations.

These fMRI studies have confirmed that high level visual areas are activated in both perception and imagery tasks. Although not identical in all cases, one could envisage a time when areas are co-activated; when seeing an occluded object for instance, where the processes of perception and imagery are needed to "complete the picture" . Here the "top down" influences may activate lower visual areas such as the primary visual cortex. Recently, Halligan et al. (1994) have proposed hallucinations may be caused when higher visual processing areas such as V4 drive lower areas (e.g. V1, dorsal LGN) via feedback connections between the areas. They cite evidence from a study with cats that shows the ability of feedback connections from V2 to drive cells in VI (Mignard and Malpeli, 1991). They argue that, in general, information found at higher levels of visual processing can influence and contribute to information processing at

lower levels.

The idea that these hallucinations are a product of activity within the visual system makes intuitive sense because the hallucinations have a similar phenomenology to normal vision, that is, the hallucinations "feel" like normal vision in a number of respects. For example, the hallucinations appear external to a person. They move and become visible suddenly without any voluntary effort while the hallucinator is alert and has his eyes open. In contrast, the everyday experience of thinking about an object is quite different. Furthermore, there is evidence that another quasi-visual process, namely mental imagery, shares a common neural substrate with visual functions (Finke, 1985; Farah et al. 1988). Since mental imagery does utilise visual processing areas, then it is even more likely that visual hallucinations share a common neural substrate with normal visual processes.

Despite the fact that not all hallucinators have identical experiences, a set of properties common to hallucinators has been established. The results from chapter 6 show that Parkinson's patients with hallucinations typically experience an image that appears while they are alert and have their eyelids open. The image suddenly becomes visible without any known trigger or voluntary effort. The image itself is generally blurry in nature, and commonly moves while being watched. The hallucinated image stays present for a period of time best characterised by hallucinators as "seconds" rather than "minutes" or "hours." The content of the hallucinations can be variable within an individual hallucinator and between hallucinators, and may include such entities as people, animals, buildings or scenery. The images may or may not be familiar to the hallucinator.

In chapter 7, an association was revealed between a certain impairments of visual perception, intact visual imagery and the complex visual hallucinations seen in Parkinson's disease hallucinations. Although controlled for in this study, overall hallucinators tend to be older than their non-hallucinating counterparts. Older adults also tend to be less efficient at binding or integrating contextual information with target memory (Chalfonte & Johnson, 1996), and age deficits in some reality monitoring tasks result from reduced accessibility of source-specifying attributes in memory, such as perceptual detail, spatial and temporal information (Johnson et al., 1995). Hallucinators exhibited an extremely low source accuracy relative to non-hallucinators and elderly controls. Failure of source monitoring and the pathology of Parkinson's disease, which is now recognised to extend beyond the nigrostriatal system and extend to dopamine deficiency in the retina (Harris, 1998), frontal lobes (Sager et al., 1988) and perhaps also in central pathways (Jellinger, 1991), may all be factors that predispose a person to hallucinations. The results of psychological testing also demonstrated that the cognitive status of Parkinsonian hallucinators can be intact. On tests that measure frontal functioning (verbal fluency), the hallucinators score on average within the normal range. Similarly, on a test that screens for cognitive impairment, hallucinators scored within the normal range. Nevertheless, other subtle deficits may be detectable with a more comprehensive test battery.

Neuropsychological batteries have associated source monitoring to the medial temporal and frontal lobes of the brain (Henkel et al., 1998). Indeed, there may be frontal damage in PD (Sagar et al., 1988, 1991). It was hypothesised in chapter 5 that the McCollough effect may be a combination of "bottom-up" and "top down" resulting in the experience of illusory colour. Indeed, the activation seen in the frontal

cortex in the McCollough effect study was attributed to "top down" processes. Hallucinations may have similar occipital and frontal components, which in some way are impaired, leading to confusion between reality and imagination.

It was asserted in the second part of this thesis that reduced or random input from the sensory system plays a role in hallucinations. The most compelling justification for this idea is that both visual and auditory hallucinations are associated with a reduction of normal sensory input in their respective sensory domains. The simple fact that these parallel phenomena exist, and further, that musical and formed auditory hallucinations can be experienced following hearing impairment (Miller and Crosby, 1979; Hammeke et al., 1983; Asaad, 1990; Berrios, 1990), suggests that hallucinations subsequent to sensory loss reveal a general property of both normal and hallucinatory perceptual processes. More specifically, the fact that individuals may experience complex well-formed perceptual experiences when peripheral sensory input, in some conditions, provides a degraded stream of information about the world, is a persuasive argument that higher level processes in the perceptual processing hierarchy can at times dominate over lower level processes involved in the various domain-specific perceptual experiences. In short, "top-down" influences appear to be important.

In chapter 6 the role of top-down processes in the production of Parkinson's disease hallucinations was discussed. In this regard, Neisser's (1976) idea of an anticipatory schema was discussed. Similarly Dennett's (1991) idea of an hypothesis generation mechanism was described. While Dennett is certainly not the first to propose the analogy between perception and hypothesis generation, he explains the concept eloquently in the following passage:

"All we need suppose must happen for an otherwise normal perceptual system to be thrown into a hallucinatory mode is for the hypothesis-generation side of the cycle (the expectation-driven side) to operate normally, while the data driven side of the cycle (the confirmation side) goes into a disordered or random or arbitrary round of confirmation and disconfirmation ..." (Dennett, 1991, p.12)

Since the hallucinating PD patients in the studies showed deficits in both perception and source monitoring, it was not possible to conclude which of these is more critical for the genesis of the visual hallucinations. Some provisional speculations are perhaps warranted, however, based upon other clinical evidence. Patients with the visual variant of Alzheimer's disease (AD), also referred to as posterior conical atrophy or the biparietal variant of AD, present with profound visual disorientation and show marked deficits on tests of visuospatial and/or perceptual ability, yet do not hallucinate (Benson et al., 1988; Mackenzie-Ross et al., 1996). Similarly, patients with semantic dementia whose knowledge base concerning the meaning of objects and faces is severely degraded in the context of marked focal temporal lobe atrophy also do not develop hallucinations (Hodges et al., 1992). It appears, therefore, that perceptual deficits alone are unlikely to be sufficient to generate the characteristic visual hallucinations found in PD.A speculative explanation would therefore be, that the combination of degraded visual information about the environment, plus impaired and perhaps fluctuating source monitoring, together with failing memory is critical for the occurrence of the visual hallucinations found in PD (see figure 8.1).

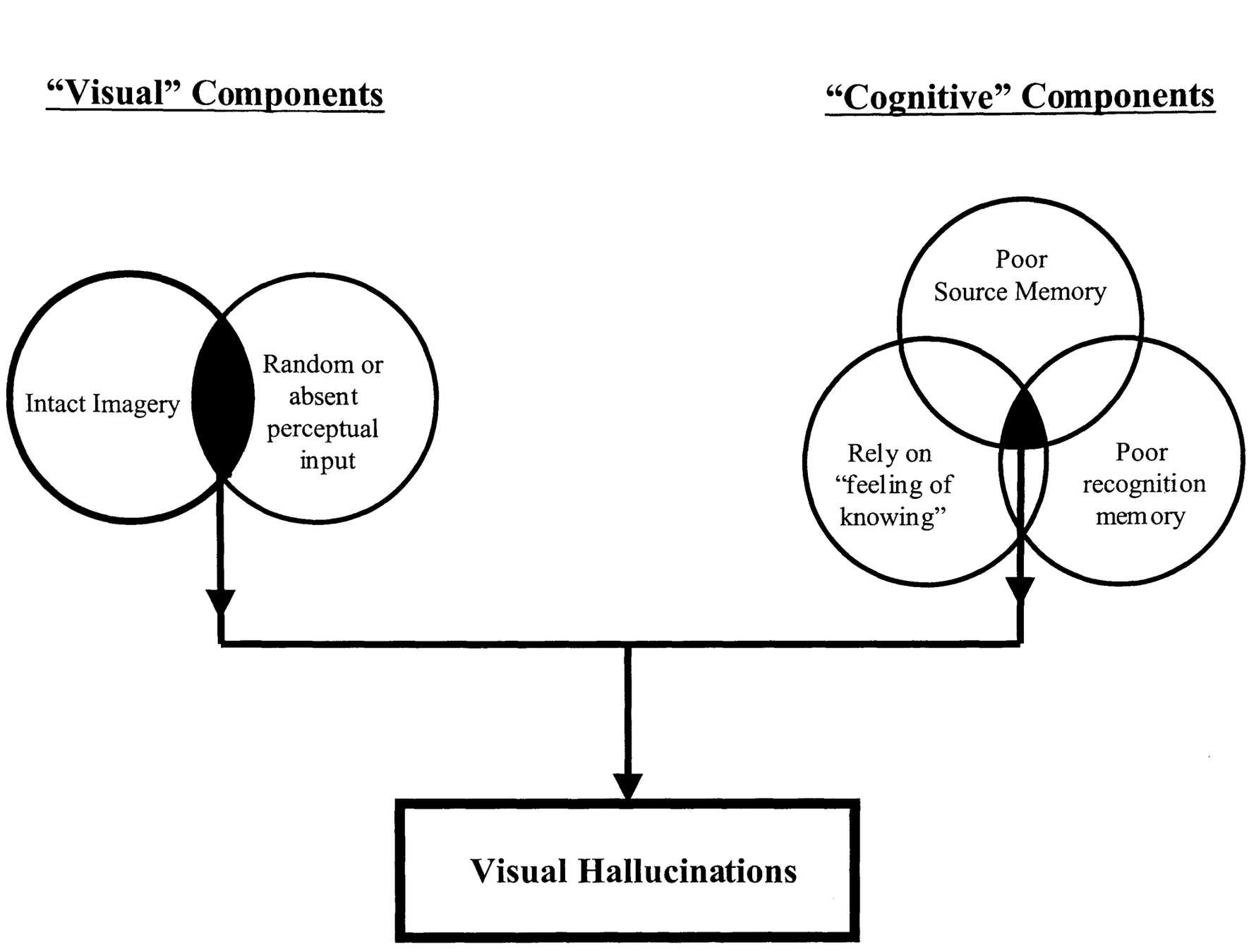


Figure 8.1: Diagram representing the components of visual hallucinations in Parkinson's disease

Future Directions

This thesis aimed to take an fMRI and neuropsychological approach to examine visual imagery and visual hallucinations in PD. Although pervious research has demonstrated a connection between perception and imagery (Farah, 1988: Kosslyn, 1994), and source monitoring has been implicated in the existence visual hallucination in certain patients (Bentall, 1990), they have drawn few conclusions on the relationship between these items and the halucinatory experience. The experiments reported here represent an initial attempt to intergrate visuoperceptual and neuropsychological finding in normal and PD patients and to asses their role in the genesis of visual hallucinations. In doing so, they have demonstrated the need for a great deal further research in a number of areas.

The model of visual hallucinations in PD speculated upon in figure 8.1 could be examined in a number of ways. First, it would be beneficial to include other clinical groups in an investigation to include patients with AD, schizophrenia and Lewy body dementia. A comparison of this type would unravel the contribution of diagnostic group, which potentially confounds the present study. It may also allow for the control or examination of medication confounds. Future studies could use a more restricted battery of tasks and a longitudinal design. A problem with correlating a large battery of tests and measurements with each other is the increased risk of type 1 errors. A strategy for examining neuropsychological and questionnaire data such as this would be to repeat the study again with larger groups. This would increase the reliability of the correlational and multivariate analysis and account for the individual differences that occur in this group of patients. A further useful development of this would then be to correlate the frequency and severity of hallucinations with the cognitive deficit

"factors or components" that arise.

The most direct assessment of top-down and bottom-up contributions could be conducted using a fMRI. Hallucinators and non-hallucinators could be pre-trained in a classical conditioning paradigm to expect a visual stimulus when a specific tone is heard. Measures of baseline activity in the visual system could quantify bottom-up contributions, and expectancy, or top-down, contributions could be assessed by measuring the effect of the tone presentation on visual system activity (assuming that the tone does indeed create an expectancy for a visual event). Short of conducting an fMRI study, a slightly more complicated signal detection study may also differentially assess the role of both top-down and bottom-up contributions. In general terms, these could be assessed by directly manipulating subjects' expectancy for a visual stimulus and also manipulating the degree to which the actual stimulus matches the expected stimulus within the same experiment.

Finally, another area for future research is in the development of effective approaches to manage the hallucinations. Regardless of whether an individual is incessantly hounded by visual images, or the person experiences the occasional hallucination, these experiences can both be frightening and annoying. Studies of the phenomenology of visual hallucinations are therefore essential, as it is only after careful, systematic examination of descriptive phenomena that patterns begin to emerge, and it is only after linking these patterns to testable hypotheses that causes can be assessed.

References

Aarsland, D., Larsen, J. P., Cumming, J. L., & Laake, K. (1999). Prevalence and clinical correlates of psychotic symptoms in Parkinson's disease. *Archieve of Neurology, 56*, 595-601.

Aggernaes, A. (1972). The difference between the experienced reality of hallucinations in young drug abusers and schizophrenic patients. *Acta Psychiatr Scan, 48*, 287-299.

Alivisatos, B., & Petrides, M. (1997). Functional activation of the Human brain during mental rotation. *Neuropsychologia., 35(2).*, 111-118.

American Psychiartic Association (1990*) DSM-IV: Diagnosic and Statistical Manual of Mental Disorders. 4th rev.* Ed Washinton, DC: American Psychiatric Press

Andersen, R. A. (1989). Visual and eye movement functions of the posterior parietal cortex. *Annual Review of Neuroscience, 12*, 377-458.

Andersen, R. A., Snowden, R. J., Treue, S., & Graziano, M. (1990). Hierarchical processing of motion in the visual cortex of monkey. *Cold Spring Harbor Symp. Quant. Biol., 55*(4), 741-748.

Andersen, R. A., & Zipser, D. (1988). The role of the posterior parietal cortex in coordinate transformations for visual-motor intergration. *Canadian Journal of Physiology and Pharmacology, 66*, 488-501.

Anderson, J. R. (1978). Arguements concerning representations for mental imagery. *Psychological Review, 85*, 249-277.

Anderson, J. R., & Bower, G. H. (1973). *Human associative memory*. New York: Winston.

Andreasen, N. C., O'Leary, D. S., Cizadlo, T., Rezai, K., Watkins, G. L., Boles-Ponto, L. L., & Hichwa, R. D. (1995a). PET studies of memory: Novel versus practised free recall of word lists. *Neuroimage, 2*, 296-305.

Andreasen, N. C., O'Leary, D. S., Cizadlo, T., Rezai, K., Watkins, G. L., Boles-Ponto, L. L., & Hichwa, R. D. (1995b). Remembering the past: Two facets of episodic memory explored with positron emission tomography. *American Journal of Psychiatry, 152*, 1576-1585.

Annett, M. (1967). The binomial distribution of right, mixed and left handedness. *Quarterly Journal of Experimental Psychology, 19*(4), 327-333.

Appell, J., Kertesz, A., & M., F. (1982). A study of language function in Alzheimer's

patients. *Brain and Language, 17*, 73-91.

Asaad, G., & Shapiro, B. (1986). Hallucinations: theoretical and clinical overview. *American Journal of Psychiatry, 143*, 1088-1097.

Bacha, H. S., Wolkowitz, O. M., Lohr, J. B., Karson, C. N., & Biegelow, L. B. (1989). High prevalence of visual hallucinations in research subjects with chronic schizophrenia. *American Journal of Psychiatry, 146*, 526-528.

Barber, T. X., & Calverley, D. S. (1964). An experimental study of "hypnotic" (auditory and visual) hallucinations. *Journal of Abnormal and Social Psychology, 63*, 13-20.

Bartolomeo, P., Bachoud-Levi, A. C., De-Gelder, B., Denes, G., Barba, G., D., Brugieres, P., & Degos, J. D. (1998). Multiple domain dissociation between impaired visiual perception and preserved mental imagery in a patient with bilateral extrastriate lesions. *Neuropsychologia, 36*(3), 239-249.

Bartolomeo, P., Bachoud-Levis, A. C., & Denes, G. (1997). Preserved imagery for colours in a patient with cerebral achromatopsia. *Cortex, 33*(2), 369-378.

Beauvois, M. F., & Saillant, B. (1985). Optic aphasia for colours and colour agnosia: A distinction between visual and visuo-verbal impairments in the processing of colours. *Cognitive Neuropsychology, 2*, 1-48.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*, 561-571.

Beson, D.F. Davis, R.J. & Snyder, B.D. (1988). Posterior cortical atrophy. *Arch Neurology, 45:* 789-793

Behrmann, M., Winocur, G., & Moscovitch, M. (1992). Dissociation between mental imagery and object recognition in a brain-damaged patient. *Nature, 359*, 636-637.

Bentall, R. P. (1990). The illusion of reality: A review and intergration of psychological research on hallucinations. *Psychological, 107*, 82-95.

Bentall, R. P., Baker, G.A., & Havers, S. (1991). Reality monitoring and psychotic hallucinations. *British Journal of Clinical Psychology, 30*, 213-222.

Bentall, R. P., & Slade, P. D. (1985). Reality testing and auditory hallucinations: A signal detection analysis. *British Journal of Clinical Psychology, 24*, 159-520.

Benton, A. L., Hamsher, K. D. S., Varney, N. R., & Spreen, O. (1983). *Contributions to neuropsychological assessment*. New York: Oxford University Press.

Berrios, G. E., & Brook, P. (1984). Visual hallucinations and sensory delusions in the elderly. *British Journal of Psychiatry, 144*, 662-664.

Bodis-Wollner, I., Bucher, S. F., Seelos, K. C., Paulus, W., Reiser, M., & Oertel, W. H. (1997). Functional MRI mapping of occipital and frontal activity during voluntary and imagined saccades. *Neurology, 49*, 416-420.

Boller, F., Passafiume, D., Keefe, N. C., Rogers, K., Morrow, L., & Kim, Y. (1984). Visuospatial impairments in Parkinson's disease: Role of perceptual and motor factors. *Archives of Neurology, 41*, 485-490.

Bonifati, M.G., Cusimoano, G., Fabrizio, E., & Vanacore, N. (1990) Hallucinations in Parkinson disease: neuropsychological study. *Ital. J. Neurol. Sci. 11*, 373-379

Bookheimer, S. Y., Zeffiro, I. A., Blaxton, T., Gaillard, W., & Theodore, W. (1995). Regional blood flow during object naming and word reading. *Human Brain Mapping, 3*(2), 93-106.

Boussaoud, D., Desimone, R., & Ungerleider, L. G. (1991). Visual tomography of area TEO in the macaque. *Journal of Comparative Neurology, 306*, 554-575.

Braddins, C. J. (1992). Dementia presenting with complex visual hallucinations. *International Journal of Geriatr. Psychiatry, 7*, 455-457.

Brammer, M., Bullmore, E. T., Simmons, A., Williams, S. C. R., Graseby, P. M., Howard, R. J., Woodruff, P. W., & Rabe-Hesketh, S. (1997). Generic brain activation mapping in fMRI: A nonparametric approach. *Magn Reson Med, 35*, 261-277

Brandt, J., Corwin, J., & Krafft, L. (1992). Is verbal recognition memory really different in Huntingtons and Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology, 14*(5), 773-784.

Brebion, G., Smith, M. J., Amador, X., Malaspina, D., & Gorman, J. M. (1998). Word recognition, discrimination accuracy and decision bias in schizophrenia: Association with positive symptomatology and depressive symptomatology. *The Journal of Nervous and Mental Disorders, 186*(10), 604-609.

Briggs, G. G., & Nebes, R. D. (1975). Patterns of hand preference in a student population. *Cortex, 11*(3), 230-238.

Broe, G. A. (1982). Parkinsonism and related disorders, *Neurological disorders in the elderly* . Bristol: Wright PSG.

Brown, R. G., & Marsden, C. D. (1986). Visuospatial function in Parkinson's disease. *Brain, 109*, 987-1002.

Brown, R. G., & Marsden, C. D. (1990). Cognitive function in Parkinson's disease: from description to theory. *Trends in Neuroscience, 13*(1), 21-29.

Bullmore, E. T., Brammer, M. J., Rabe-Hesketh, S., Curtis, V. A., Morris, R. G., Williams, S. C. R., Sharma, T., & McGuire, P. K. (1999). Methods for diagnosis and treatment of stimulus-correlated motion in generic brain activation studies using fMRI. *Human Brain Mapping, 7*, 38-48.

Bullmore, E. T., Brammer, M. J., Williams, S. C. R., Rabe-Hesketh, S., Janot, N., David, A. S., Mellers, J. D. C., Howard, R., & Sham, P. (1996). Statistical methods of estimation and inference for functional MR image analysis. *Mag. Res. Med, 35*, 261-277.

Burton, L. A., Wagner, N., Lim, C., & Levy, J. (1992). Visual field differences for clockwise and counterclockwise mental rotation. *Brain and Cognition, 18*, 192-207.

Butters, N., & Barton, M. (1970). Effect of parietal lobe damage on the performance of reversible operations in space. *Neuropsychologia, 8*(2), 205-214.

Butters, N., Barton, M., & Brody, B. (1970). Role of the right parietal lobe in the mediation of cross-model associations and reversible operations in space. *Cortex, 6*, 174-190.

Celesia, G. G., & Barr, A. N. (1970). Psychosis and other psychiatric manifestations of levodopa therapy. *Arch Neurol, 23*, 193-200.

Chalfonte, B. L., & Johnson, M. K. (1996). Feature memory and binding in young and older adults. *Memory and Cognition, 24*, 403-416.

Chao, L. L., & Martin, A. (1999). Cortical regions associated with perceiving, naming and knowing about colors. *Journal of Cognitive Neuroscience, 11*(1), 25-35.

Charcot, V., Tzourio, N., Zilbovicius, M., Mazoyer, B., & Denis, M. (1992). Different mental imagery abilities result in different regional cerebral blood flow activation patterns during cognitive tasks. *Neuropsychologia, 30*, 565-580.

Chatterjee, A., & Southwood, M. H. (1985). Cortical blindness and visual imagery. *Neurology, 45*(12), 2189-2195.

Clark, H. H., & Chase, W. G. (1972). On the process of comparing sentences against pictures. *Cognitive Psychology, 3*(3), 472-517.

Cohen, M., Kosslyn, S., Breiter, H., DiGolamo, G., Thompson, W., Anderson, K., Bookheimer, S., Rosen, B., & Belliveau, J. (1996). Changes in cortical activity during mental rotation: A mapping study using functional MRI. *Brain., 119.*, 89-100.

Cohen, W., & Polich, J. (1989). No hemispheric differences for mental rotation of letters or polygons. *Bulletin of the Psychonomic Society, 27*(1), 25-28.

Cooper, L. A. (1975). Mental rotation of randon two-dimentional shapes. *Cognitive Psychology, 7*, 20-43.

Cooper, L. A. (1976). Demonstration of a mental analog of an external rotation. *Perception and Psychophysics, 19*, 296-302.

Cooper, L. A., & Podgorny. (1976). Mental transformations and visual comparisons processes: Effects of complexity and similarity. *Journal of Experimental Psychology: Human Perception and Performance*(2), 503-514.

Cooper, L. A., & Shepard, R. N. (1975). Mental transformations in the identification of left and right hands. *Journal of Experimental Psychology: Human Perception and Performance, 1*, 48-56.

Cooper, L. A., & Shepard, R. N. (Eds.). (1973). *Chronometric studies of the rotation of mental images*. New York: Academic press.

Corballis, M. C., & Sergent, J. (1989). Mental rotation in a commissurotomized subject. *Neuropsychologia, 26*, 13-26.

Corballis, M. C., & Sidey, S. (1993). Effects of concurrent memory load on visual field differences in mental rotation. *Neuropsychologia, 31*(3), 183-197.

Corbetta, M., Miezin, F. M., Dobmeyer, S., Shulman, G. L., & Petersen, S. E. (1991). Selective and divided attention during visual discriminations of shape, color and speed: Functional anatomy by positron emmision tomography. *The Journal of Neuroscience, 11(8)*, 2383-2402.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. (1998). An area specialized for spatial working memory in human frontal cortex. *Science, 279*, 1347-1351.

Cowin, J. (1994). On measuring disrimination and response bias: Unequal number of targets and distractors and two classes of distractors. *Neuropsychology, 8*(1), 110-117.

Craik, K. J. W. (1940). Origin of visual after-images. *Nature, 145*(512).

Dallos, V., Heathfield, K., Stone, P., & Allen, F. (1972). The comparative value of amantidine and levodopa. *Postgrad. Med. Journal, 48*, 354-358.

Damasio, A. (1989). A system-level proposal for the neuronal substrates of recall and recognition. *Cognition, 33*, 1063-1071.

Damasio, A. R., Yamada, T., Damasio, H., Corbett, J., & McKee, J. (1980). Central achromatopsia: Behavioural, anatomic and psysiologic aspects. *Neurology, 30*, 1064-1071.

David, A. S. (1994). The neuropsychological origin of auditory hallucinations. In A. S. David & J. C. Cutting (Eds.), *The neuropsychology of schizophrenia* . Hove, UK: Lawrence Erlbaum.

Davidoff, J. (1991). *Cognition through Color*. Cambridge, Mass: The MIT Press.

Davidoff, J., & Wilson, B. (1985). A case of visual agnosia showing a disorder of pre-semantic visual classification. *Cortex, 21*(1), 121-134.

De Jong, B. M., Shipp, S., Skidmore, B., Frackowiak, R. S. J., & Zeki, S. (1994). The cerebral activity related to the visual perception of forward motion in depth. *Brain, 117*, 1039-1054.

De Renzi, E., & Faglioni, P. (1967b). The relationship between visuospatial impairment and constructional apraxia. *Cortex, 3*, 327-342.

De Renzi, E., Faglioni, P., & Villa, P. (1977). Topographical amnesia. *Journal of Neurology, Neurosurgery and Psychiatry, 40*, 498-505.

De Renzi, E., & Saetti, M. C. (1997). Associative agnosia and optic aphasia:qualitative or quantative difference? *Cortex*(33), 115-130.

De Renzi, E., & Spinnler, H. (1967a). Impaired performance on colour tasks in patients with hemispheric damage. *Cortex, 3*, 194-217.

De Valois, R. L., Abramov, I., & Mead, W. R. (1967). Single cell analysis of wavelength discrimination at the lateral geniculate nuclueus in the macaque. *Journal of Neurophysiology, 30*(3), 415-433.

De Vreese, L. P. (1991). Two systems for colour naming deficits. Verbal disconnection versus the colour imagery disorder. *Neuropsychologia, 29*, 1-18.

De Vreese, L. P. (1988). Category-specific versus modality-specific aphasia for colours: A review of the pioneer case studies. *International Journal of Neurosciences, 43*, 195-206.

Decety, J., Kawashima, R., Gulyas, B., & Roland, P.E. (1992) Preparation for reaching: a PET study of the participating structures in the human brain. *NeuroReport, 3(9),* 761-764

Dennett, D. (1991). *Consciousness Explained.* Toronto: Little Brown and Company.

Desimone, R., & Ungerleider, L. G. (1986). Multiple visual areas in the caudal superior temporal sulcus of the macaque. *Journal of Comparative Neurology, 248*(2), 164-189.

DeSmet, Y., Ruberg, M., Serdaru, M., Dubois, B., Lhermitte, F., & Agid, Y. (1982). Confusion, dementia and anticholinergics in Parkinson's disease. *Journal of*

Neurology, Neurosurgery and Psychiatry, 45, 1161-1164.

D'Esposito, M., Detre, J. A., Aguirre, G. K., Stallcup, M., Alsop, D. C., Tipett, L. J., & Farah, M. (1997). A functional MRI study of mental image generation. *Neuropsychologia, 35*, 725-730.

Deutsch, G., Bourbon, A., Papanicolaou, C., & Eisenberg, M. (1988). Visiospatial tasks compared via activation of regional cerebral blood flow. *Neuropsychologia, 26*, 445-452.

Deweert, C. M., & Levelt, W. J. (1976). Comparison of normal and dichoptic colour mixing. *Vision Research, 16*(1), 59-70.

Dijkerman, C. H., & Milner, D. A. (1997). Copying without perceiving: Motor imagery in visual form agnosia. *NeuroReport, 8*, 729-732.

Ditunno, P. L., & Mann, V. A. (1990). Right hemisphere specialization for mental rotation in normals and brain damaged subjects. *Cortex, 26*, 177-188.

Dodwell, P. C., & Humphrey, G., K. (1990). A functional theory of the McCollough effect. *Psychological Review, 97*(1), 78-89.

Dolan, R. J., Fink, G. R., Booth, M., Holmes, A., Frackowiak, R. S. J., & Friston, K. J. (1997). How the brain learns to see objects and faces in an impoverished context. *Nature, 389*, 596-599.

Donders, F. C. (1969). Over de snelheid van psychisce processen. In W. G. Koster (Ed.), *Attention and Performance II* (pp. 412-431). Amsterdam: North-Holland (Original work published in 1868).

Dowling, J. E. (1967). The site of visual adaptation. *Science, 155*(3760), 273-279.

Dubois, B., Pillon, B., Legault, F., Agid, Y., & Lhermitte, F. (1988). Slowing of cognitive processing in progressive supranuclear palsy: A comparison with Parkinson's disease. *Archieves of Neurology, 45*, 1194-1199.

Engel, S., Zhang, X., & Wandell, B. (1997). Colour tuning in human visual cortex measured with functional magnetic resonance imaging. *Nature, 338*, 68-71.

Farah, M. J. (1984). The neurological basis of mental imagery: A componential analysis. *Cognition, 18*, 245-272.

Farah, M. J., Hammond, K. M., Levine, D. N., & Calvanio, R. (1988). Visual and spatial mental imagery: Dissociable systems of representation. *Cognitive Psychology, 20*, 439-462.

Feenan, K., & Snodgrass, J. G. (1990). The effect of context on discrimination and bias

in recognition memory for pictures and words. *Memory and Cognition, 18*(5), 515-527.

Feinberg, W., & Rapcsack, S. (1989). Peduncular hallucinosis following paramedian thalamic infarction. *Neurology, 39*, 1535-1536.

Felleman, D. J., & Van Essen, D. C. (1991). Distributed hierarchial processing in the primate cerebral cortex. *Cerabral Cortex, 1*, 1-47.

Findley, L. J. (1993). Tremors: differential diagnosis and pharmacology. In J. Jankovic & E. Tolosa (Eds.), *Parkinson's Disease and Movement Disorders 2nd ed* . Baltimore: Williams & Wilkins.

Fink, G. R., Markowitsch, H. J., Reinkemeier, M., Bruckbauer, T., Kessler, J., & Heiss, W. D. (1996). Cerebral representation of one's own past: Neural networks involved in autobiographical memory. *Journal of Neuroscience, 16*, 4275-4282.

Finke, R. A. (1985). Theories relating mental imagery to perception. *Psychological Bulletin, 98*(236-259).

Finke, R. A. (1989). *Principles of mental imagery*. Cambridge: MIT Press.

Finke, R. A., Johnson, M. K., & Shyi, G. C. W. (1988). Memory confusions for real and imagined completions of symmetrical visual patterns. *Memory and Cognition, 16*, 133-137.

Fischer, S. C., & Pellegrino, J. W. (1988). Hemispheric differences for components of mental rotation. *Brain and Cognition, 7*, 1-15.

Flavell, J. H. (1979). Metacognition and cognitive monitoring: A new area of cognitive developmental enquiry. *American Psychologist, 34*(10), 906-911.

Fletcher, P. C., Frith, C. D., Baker, S. C., Shallice, T., Frackowiak, R. S., & Dolan, R. J. (1995). The mind's eye-precuneus activation in memory-related imagery. *Neuroimage, 2*, 195-200.

Folstein, M., Folstein, S., & McHugh, P. (1975). "Mini-Mental State". *Journal of Psychiatric Research, 12*, 189-198.

Friston, K., J., Williams, S. C. R., Howard, R., Frackowiak, R. S. J., & Turner, R. (1996). Movement-related effects in fMRI time-series. *Magnetic Resonance in Medicine, 35*, 346-355.

Friston, K. J., Frith, C. D., Liddle, P. F., & Frackowiak, R. S. (1991). Comparing functional PET images: The assessment of significant change. *Journal of Cerebral Blood Flow Metabolism, 11*, 690-699.

Frith, C. D. (1992). *The cognitive neuropsychology of schizophrenia.* Hillsdale, NJ.: Lawrence Erlbaum.

Galton, F. (1883). *Inquires into Human Faculty and its Development.* London: Macmillan.

Gardiner, J. M. (1988). Functional aspects of recollective experience. *Memory and cognition, 16*, 309-313.

Gardiner, J. M., & Java, R. I. (1989). Recollective experience in word and nonword recognition. *Memory and Cognition, 18*(1), 23-30.

Gardiner, J. M., & Parkin, A. J. (1990). Attention and recollective experience in recognition memory. *Memory and Cognition, 18*(6), 579-583.

Gellar, T. J., & Bellur, S. N. (1987). Penducular hallucinosis: magnetic resonance imaging confirmation of mesencephalic infaction during life. *Annuals of Neurology, 21*, 602-604.

Gibb, W. R. G. (1992). Neuropathology of Parkinson's disease and related syndromes. In J. M. Cerarbaum & S. T. Gancher (Eds.), *Neurologic Clinics, Parkinson's Disease* (Vol. 10, pp. 361-376): Harcourt Brace Javanovich.

Gibb, W. R. G. (1993). Biochemical and Functional Organisation of the Basal Ganglia. In J. M. Cedarbaum & S. T. Gancher (Eds.), *Neurologic Clinics* (Vol. 10, pp. 361-376): Harcourt Brace Jovanovich.

Gibb, W. R. G., Esiri, M. M., & Lees, A. J. (1987). Clinical and pathological features of diffuse cortical Lewy body disease (Lewy body dementia). *Brain, 110*, 1131.

Gibb, W. R. G., & Lee, A. J. (1988). The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry, 51*, 745-752.

Girotti, F., Soliveri, P., Carella, F., & et al. (1988). Dementia and cognitive impairment in Parkinson's disease. *Journal Neurol Neurosurg Psych, 51*, 1498-1502.

Glantz, R.H., Bieliauskas, L., & Paleologos N. (1986) Behavioral Indicators of hallucinosis in Levodopa-treated Parkinson's disease. *Advances in Neurology, 45*, 417-420

Goetz, C. G. (1992). The historical background of behavioural studies in Parkinson's disease. In S. J. Huber & J. L. Cummings (Eds.), *Parkinson's Disease, Neurobehavioural Aspects* . New York: Oxford University Press.

Goetz, C. G., Pappert, E. J., Blasucci, L. M., Stebbins, G. T., Ling, Z. D., Nora, M. V., &

Carvey, P. M. (1998). Intravenous levodopa in hallucinating Parkinson's disease patients: High dose challenge does not precipitate hallucinations. *Neurology, 50*, 515-517.

Goetz, C.G., & Stebbins. (199) Risk factors for nursing home placement in advanced Parkinson's disease. *Neurology, 43*, 2227-2229

Goetz, C.G., & Stebbins. (1995) Mortality and hallucinations in nursing home patients with advanced Parkinson's disease. *Neurology, 45*, 669-671

Goldenberg, G. (1992). Loss of visual imagery and loss of visual knowledge: A case study. *Neuropsychologia, 30*, 1081-1099.

Goldenberg, G., Mullbacher, W., & Nowak, A. (1995). Imagery without perception- A case study of anosognosia for cortical blindness. *Neuropsychologia, 33*, 1373-1382.

Goldenberg, G., Podreka, I., Steiner, M., & Willmes, K. (1987). Patterns of regional blood flow related to memorising of high and low imagery words. An emission computer tomography study. *Neuropsychologia, 30*, 1081-1099.

Goldenberg, G., Podreka, I., Steiner, M., Willmes, K., Suees, E., & Deecke, L. (1989). Regional cerebral blood flow patterns in visual imagery. *Neuropsychologia, 27*, 641-664.

Gomori, A. J., & Hawryluk, G. A. (1984). Visual agnosia without alexia. *Neurology, 34*, 947-950.

Goodale, M. A., Milner, A. D., Jakobson, L. S., & Carey, D. P. (1991). A neurological dissociation between perceiving objects and grasping them. *Nature, 349*, 154-156.

Goodkin, D. A. (1980). Mechanisms of bromocriptine-induced hallucinations (letter). *New England Journal Medicine, 302*, 1479.

Graham, J. M., Grunewald, R. A., & Sagar, H. J. (1997). Hallucinosis. *Journal of Neurology, Neurosurgery, and Psychiatry, 63*, 434-440.

Granit, R. (1938). Processes of adaptation in the vertebrate retina in the light of recent photochemical and electrophysiological research. *Documenta Ophthalmologica, 1*, 7-77.

Gulyas, B., & Roland, P. E. (1994). Processing and analysis of form, colour and binocular disparity in the human brain. Functional anatomy by positron emission tomography. *European Journal of Neuroscience, 8*, 2229-2231.

Gurd, J. M., & Ward C.D. (1989). Retrieval from semantic and letter initial categories in Patients with Parkinson's disease. *Neuropsychologia, 27*(5), 743-746.

Hadano, K. (1984). On block design constructional disability in right and left hemisphere brain-damaged patients. *Cortex, 20*(3), 391-401.

Hadjikhani, N., Liu, A. K., Dale, A. M., Cavanagh, P., & Tootell, R. B. (1998). Retinotopy and color sensitivity in human visual cortical area V8. *Nature Neuroscience, 1*(3), 235-241.

Halligan, P. W., Marshall, J. C., & Ramachandran, V. S. (1994). Ghosts in the machine: a case discription of visual and haptic hallucinations after right hemisphere stroke. *Cognitive Psychology, 11*, 459-477.

Hammeke, T. A., McQuillen, M. P., & Cohen, B. A. (1983). Musical hallucinations associated with acquired deafness. *Journal of Neurology, Neurosurgery, Psychiatry, 46*, 570-572.

Hanley, J. R., Dewick, H. C., Davis, A. D., & Playfer, J. (1990). Verbal fluency in Parkinson's disease. *Neuropsychologia, 28*, 737-741.

Harris, C. S., & Gibson, A. R. (1968). Is orientation-specfic color adaptation in human vision due to edge detectors, afterimages, or "dipoles". *Science, 162*, 1506-1507.

Harris, J. P. (1998). Vision in Parkinson's disease: what are the deficits and what are their origins. *Neuro-Ophthalmology*, 113-135.

Harvey, N. S. (1986). Psychiatric disorders in Parkinsonism: Organic cerebral states and drug reactions. *Psychomatics, 27*(3), 175-184.

Hashtroudi, S., Johnson, M. K., & Chrosniak, l. D. (1990). Aging and qualitative characteristics of memories for perceived and imagined complex events. *Psychology and Aging, 5*, 119-126.

Haug, B. A., Baudewig, J., & Paulus, W. (1998). Selective activation of human cortical area V5 by a rotating visual stimuus in fMRI: implication of attentional mechanisms. *NeuroReport, 9*, 611-614.

Haxby, J. V., Grady, C. L., Horwitz, B., Ungerleider, L. G., MIshkin, M., Carson, R. E., Herscovitch, P., Schapiro, M. B., & Rapoport, S. I. (1991a). Dissociation of object and spatial visual processing pathways in the human extrastriate cortex. *Proc. Natl. Acad. Sci. USA, 88*, 1621-1625.

Haxby, J. V., Grady, C. L., Ungerleider, L. G., & Horwitz, B. (1991b). Mapping the functional neuroanatomy of the intact brain with brain works imaging. *Neuropsychologia, 29*(6), 539-555.

Hecht, S. (1928). On the binocular fusion of colors and its relation to the ories of color

vision. *Proceeding of the National Academy of Sciences, 14*, 237-240.

Hecht, S., Haig, C., & Chase, A. M. (1937). The influence of light adaption on subsequent dark adaption of the eye. *Journal of General Physiology, 20*, 831-850.

Heeske-Dewick, H. (1995). Hallucinations in Parkinson's disease: Characteristics and associated clinical features. *International Journal of Geriatric Psychiatry, 19*, 487-495.

Heilburn, A.B. (1980) Impaired reognition of self-expressed thought in patients with auditory hallucinations. *Journal of Abnormal Psychology, 89,* 728-736

Henkel, L. A., Johnson, M. K., & De Leonardis, D. M. (1998). Aging and source monitoring: Cognitive processes and neuropsychological correlates. *Joutrnal of Experimental Psychology: General, 127*(3), 251-268.

Heywood, C., & Cowey, A. (1998). With color in mind. *Nature Neuroscience, 1*(3), 171-172.

Heywood, C. A., Gadotti, A., & Cowey, A. (1992). Cortical area V4 and its role in the perception of color. *The Journal of Neuroscience, 12(10)*, 4056-4085.

Hirst, W. (1989). On consciousness, recall, recognition, and the architecture of memory. In S. Lewandowsky, J. C. Dunn, & et al. (Eds.), *Implicit memory: Theoretical issues* (pp. 33-46). Hillsdale N.J USA: Lawrence Erlbaum Associates.

Hoch, H. S., & Tromley, C. L. (1978). Mental rotation and perceptual uprightness. *Perception and Psychophysics, 24*, 529-533.

Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: onset, progression, and mortality. *Neurology, 17*, 427-442.

Hodges, J.R., Patterson, K., Oxbury, S. et al., (1992) Semantic dementia. Progressive fluent aphasia with temporal lobe atrophy. *Brain, 115,* 1783-1806

Holroyd, S., Rabins, P., Finkelstein, D., Nicolson, M. C., Chase, G. A., & Wisniewski, S. C. (1992). Visual hallucinations in patients with muscular degeneration. *American Journal of Psychiatry, 149*, 1701-1706.

Hoptman, M. J., & Davidson, R. J. (1994). How and why do the two cerebral hemispheres interact. *Psychological Bulletin, 116*(2), 195-219.

Horiguchi, J., Nishimatsu, O. Inami, Y., Sukegawa, T. & Shoda, T (1991). A clinical study on intellectual impariment in Parkinsonian patients during long-term treatment. *Jap J. Psychiat. Neurol. 45(1)* 13-18

Horrax, G. (1923). Visual hallucinations as a cerebral localizing phenomenon with

special reference to their occurence in tumors of the temporal lobe. *Archives of Neurology and Psychiatry, 10*, 532-547.

Horrowitz, M. J. (1975). Hallucinations: An information-processing approach. In R. K. Siegel & L. J. West (Eds.), *Hallucinations: Behaviour, experience and theory* (pp. 163-196). New York: Wiley.

Howard , R., & Levy, R. (1994). Charles Bonnet syndrome plus: complex visual hallucinations of Charles Bonnet syndrome type in late paraphrenia. *International Journal of Geriatric Psychiatry, 9*, 399-404.

Howard, R., Brammer, M., Wright, I., Woodruff, P. W. R., Bullmore, E., & Zeki, S. (1996). A direct demonstration of functional specialization within motion-related visual and auditory cortex of the human brain. *Current Biology, 6(8)*, 1015-1019.

Howard, R., ffytche, D. H., Barnes, J., McKeefry, D., Ha, Y., Woodruff, P. W., Bullmore, E. T., Simmons, A., Williams, S. C. R., David, A. S., & Brammer, M. (1998). The functional anatomy of imaging and perceivng colour. *Neuroreport, 9*, 1019-1023.

Howard, R., Williams, S. C. R., Bullmore, E., Brammer, M., Mellers, J. D. C., Woodruff, P. W. R., & David, A. S. (1995). Cortical response to exogenous visual stimulation during visual hallucinations. *The Lancet, 345*, 70.

Howard, R. J., Bullmore, M., Brammer, M., Williams, S. C. R., Mellers, J., Woodruff, P., David, A., Andrew, C., Allin, M., Simmons, A., & Cox, T. (1995). Activation of area V5 by perception of motion demonstrated with echoplanar MR imaging. *Magnetic Resonance Imaging, 13*(6), 907-909.

Hughes, A. J., Daniel, S. E., & Lee, A. J. (1992). Parkinsionism: onset, progression and mortatility. *Archives of Neurology.*

Humphrey, G. K., Goodale, M. A., & Gurnsey, R. (1991). Orientation discrimination ina visual form agnosia: Evidence from the McCollough effect. *Psychological Science, 5*, 331-335.

Humphrey, G. K., Goodale, M. A. G., Corbetta, M., & Aglioti, S. (1995). The McCollough effect reveals orientation discrimination in a case of cortical blindness. *Current Biology, 5*, 545-551.

Humphrey, G. W., & Riddoch, M. G. (1987). *To see but not to see - a case study of visual agnosia.* London, Hillsdale, NJ: Lawrence Erlbaum.

Intons-Peterson, M. J. (1983). Imagery paradigms: How vulnerable are they to

experimenters' expectations? *Journal of Experimental Psychology: Human Perception and Performance, 9*, 394-412.

Inzelberg, R., Kipervasser, S., & Korczyn, A.D. (1998) Auditory hallucinations in Parkinson's disease. *J of Neurol Neurosurg Psychiatry,* 64, 533-535

James, T. W., Humprey, G. K., Gati, J. S., Menon, R. S., & Goodale, M. A. (1998,). *The McCollough effect produces increased fMRI signal in the fusiform and lingual gyri.* Paper presented at the 4th International Conference on Functional Mapping of the Human Brain, Montreal, Canada.

Jankowiak, J., Kinsbourne, M., Shalev, R. S., & Bachman, D. L. (1992). Preserved visual imagery and categorization in a case of associative visual agnosia. *Journal of Cognitive Neuroscience, 4*, 119-131.

Jarvik, M. (1970). *Drugs, hallucnations and memory*. New York: Plenum.

Jellinger, K.A. (1991) Pathology of Parkinson's disease. Changes other than the nigrostriatal pathway. *Mol. Chem Neuropathol. 144,* 153-197.

Jellinger, K., & Riederder, P. (1984). Dementia in Parkinson's disease and (Pre) Senile Dementia of the Alzheimer Type (Morphological Aspects and Changes in the Intracerebral MAO Activity). In R. G. Hassler & J. F. Christ (Eds.), *Advances in Neurology* (Vol. 40, pp. 199-210). New York: Raven Press.

Johnson, M. K. (1991). Reality monitoring: evidence from confabulation in organic brain disease patients. In G. P. Prigatano & D. L. Schacter (Eds.), *Awareness of deficit after brain injury* . New York: Oxford University Press.

Johnson, M. K. (1988). Reality monitoring: An experimental phenmenological approach. *Journal of Experimental Psychology, 117*, 390-394.

Johnson, M. K., De Leonardis, D. M., Hashtroudi, S., & Ferguson, S. A. (1995). Aging and single versus multiple cues in source monitoring. *Psychology and Aging, 10*, 507-517.

Johnson, M. K., Hashtroudi, S., & Lindsay, D. S. (1993). Source monitoring. *Psychological Bulletin, 114*, 3-28.

Johnson, M. K., Kounios, J., & Reeder, J. A. (1994). Time-course studies of reality monitoring and recognition. *Journal of Experimental Psychology, 20*, 1409-1419.

Johnson, M. K., & Raye, C. L. (1981). Reality monitoring. *Psychological Review, 88*, 67-85.

Kawashima, R., O'Sullivan, B. T., & Roland, P. E. (1995). Positron-emission

tomography studies of cross-modality inhibition selective attentional tasks- closing the mind's eye. *Proc. Natl. Acad, Sci. USA, 92*(13), 5969-5972.

Kim, E. (1993). Management of psychiatric disorders in epileptic patients. *New Dir Ment Health Serv, 57*, 99-108.

Kiyosawa, M., Inoue, C., Kawasaki, T., Tokoro, T., Ishii, K., Ohyama, M., Senda, M., & Soma, Y. (1996). Functional neuroanatomy of visual object naming: A PET Study. *Graf's Archieve for Clinical and Experimental Ophthalmology, 234*, 110-115.

Klawans, J. (1988). Psychiatric side effects during the treatment of Parkinson's disease. *Journal of Neural Transmission, 27*, 117-122.

Klein, C., Kompf, D., Pulkowski, U., Moser, A., & Vieregge, P. (1997) A study of visual hallucinations in patients with Parkinson's disease. *J. Neurol. 144*, 371-377

Kleinschmidt, A., Lee, B. B., Requardt, M., & Frahm, J. (1996). Functional mapping of color processing by magnetic resonance imaging of responses to selective P- and M-pathway stimulation. *Exp. Brain. Res, 110*, 279-288.

Kosslyn, S. (1980). *Image and Mind.* Cambridge: Harvard University Press.

Kosslyn, S. (1994). *Image and Brain: The resolution of the imagery debate.* Cambridge: The MIT Press.

Kosslyn, S., & Schwartz, S. P. (1977). A simulation of visual imagery. *Cognitiive Science, 1*, 265-295.

Kosslyn, S. M. (1983). *Ghost's in the mind's machine.* Cambridge, Mass.: Harvard University Press.

Kosslyn, S. M., Alpert, N. M., Thompson, W. L., Maljkovic, S. B., Weise, C. F., Chabris, S. E., Hamilton, S. E., Rauch, S. L., & Buonanno, F. S. (1993). Visual mental imagery activates topographically organised visual cortex: PET investigations. *Journal of Cognitive Neuroscience, 5*, 263-287.

Kosslyn, S. M., Digirolamo, G. J., Thompson, W. L., & Alpert, N. M. (1998). Mental rotation of objects versus hands: Neural mechanisms revealed by positron emission tomography. *Psychophysiology, 35*, 151-161.

Kosslyn, S. M., & Ochsner, K. N. (1994). In search of occipital activation during visual mental imagery. *Trends in Neuroscience, 17(7)*, 290-291.

Kosslyn, S. M., & Pomerantz, J. R. (1977). Imagery, propositions, and the form of internal representations. *Cognitive Psychology, 9*, 52-76.

Kosslyn, S. M., Shin, L. M., Thompson, W. L., McNally, R. J., Rauch, S. L., Pitman, R.

K., & Alpert, N. M. (1996). Neural effects of visualizing and perceiving aversive stimuli: a PET investigation. *NeuroReport, 7(10)*, 1569-1576.

Kosslyn, S. M., Thompson, W. L., Kim, I. J., & Alpert, N. M. (1995). Topographical representations of mental images in primary visual cortex. *Nature, 378*, 496-498.

Kulikowski, J. J., Walsh, V., McKeefry, D. J., Butler, S. R., & Carden, D. (1994). The electrophysiological basis of colour processing in macaques with V4 lesions. *Behav. Brain Res, 60*, 73-78.

Lange, N. (1996). Statistical approaches to human brain mapping by functional magnetic resonance imaging. *Stat. Med., 15*(4), 389-428.

Lanska, D., Lanska, M., & Mendez, M. (1987). Brainstem auditory hallucinations. *Neurology, 35*, 1685.

Le Bihan, D., Turner, R., Zeffiro, T. A., Cuenod, C. A., Jezzard, P., & Bonnerot, V. (1993). Activation of human primary human cortex during visual recall: A magnetic resonance imaging study. *Proceedings of the National Academy of Science USA, 90*, 11802-11805.

Lerner, A., Koss, E., Patterson, M. B., Ownby, R. L., Hedera, P., Friedland, R. P., & Whitehouse, P. J. (1994). Concomitants of visual hallucinations in Alzheimer's disease. *Neurology, 44*, 523-527.

Levine, D. N., Warach, J., & Farah, M. J. (1985). Two visual systems in mental imagery: A dissociation of "what" and "where" in imagery disorders due to bilateral posterior cerebral lesions. *Neurology, 35*, 1010-1018.

L'Hermitte, J. (1922). Syndrome de la callotte du padoncle cerebral. Les troubles psycho-sensorieles dans les lesions du mesencephale. *Revue Neurologigue, 38*, 1359-1365.

Libermann, A., Dziatolowski, M., Wang, C. C., & et al. (1979). A prevalence survey of Parkinson's disease and other movement disorders in the People's Republic of China. *Achives of Neurology, 42*, 655-657.

Livingstone, M., & Hubel, D. (1988). Segregation of form, colour, movement, and depth: Anatomy, psysiology and perception. *Science, 240*, 740-749.

Livingstone, M. S., & Hubel, D. H. (1984). Anatomy and physiology of a color system in the primate visual cortex. *Journal of Neuroscience, 4*, 309-356.

Loranger, A. W., Goodell, H., McDowell, F. H., Lee, J. E., & Sweet, R. D. (1973). Parkinsonism, L-Dopa and intelligence. *Am. J. Psychiatry, 130*(12), 1386-1389.

Lueck, C. J., Zeki, S., Friston, K. J., Deiber, M. P., Cope, P., Cunningham, V. J.,

Lammertsma, A. A., Kennard, C., & Frackowiak, R. S. J. (1989). The colour centre in the cerebral cortex of man. *Nature, 340*, 386-389.

Mackay, D. M., & Mackay, V. (1973). What causes decay of pattern-contingent chromatic aftereffects? *Vision Research, 15*, 462-464.

Mackenzie-Ross, S.J., Graham, N., & Stuart-Green, L., et al., (1996) Progessive biparietal atrophy: an atypical presentation of Alzheimer's disease. *Journal of Neurology Neurosurgery & Psychiatry 61,* 388-395

Mandler, G. (1980). Recognizing: the judgement of previous occurences. *Psychological Review, 87*(3), 379-388.

Manford, M., & Andermann, F. (1998). Complex visual hallucinations. *Brain, 121*, 1819-1840.

Mantyla, T. (1993). Knowing but not remembering: adult age differences in recollective experience. *Memory and Cognition, 21*(3), 379-388.

Marks, D. F. (1973). Visual imagery differences in the recall of pictures. *British Journal of Psychology, 64*(1), 17-24.

Marsden, C. D. (1994). Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry, 57*, 672-681.

Marsden, C. D. (1989). Slowness of movement in Parkinson's disease. *Movement Disorders, 4*(Supplement 1), 26-37.

Martin, A., & Fedio, P. (1983). Word production and comprehension in Alzheimer's disease: The breakdown of semantic knowledge. *Brain and Language, 19*, 124-141.

Martin, A., Haxby, J. V., Lalonde, F. M., Wiggs, C. L., & Ungerleider, L. G. (1995). Discrete cortical regions associated with knowledge of color and knowledge of action. *Science, 270*, 102-105.

Martin, A., Wiggs, C. L., Ungerleider, L. G., & Haxby, J. V. (1996). Neural correlates of category-specific knowledge. *Nature, 379*, 649-652.

Mayeux, R., Stern, Y., Rosenstein, R., Marder, K., & et al. (1988). An estimate of the prevalence of dementia in idiopathic Parkinson's disease. *Archives of Neurology, 45*(3), 260-262.

Maylor, E. A. (1995). Remembering versus knowing television theme tunes in middle-aged and elderly adults. *British Journal of Psychology, 86*, 21-25.

McCollough, C. (1965). Color adaption of edge-detectors in the human visual system. *Science, 149*, 1115-1116.

McGuire, P. K., Silbersweig, D. A., Wright, I., Murray, R. M., David, A. S., Frackowiak, R. S., & Frith, C. D. (1995). Abnormal monitoring of inner speech: A physiological basis for auditory hallucinations. *Lancet, 346*, 596-600.

McIntyre, J. S., & Craik, F. I. M. (1987). Age differences in memory for item and source information. *Canadian Journal of Psychology, 41*, 175-192.

Mckee, A. C., Levine, D. N., Kowall, N. W., & Richardson, E. P. J. (1990). Penduncular hallucinosis associated with isolated infartion of the substantia nigra pars reticulata. *Ann Neurol, 27*, 500-504.

McKeefry, D., & Zeki, S. (1997). The position and topography of the human colour centre as revealed by functional magnetic resonance imaging. *Brain, 120*, 2229-2242.

McKeith, I. G., Perry, R. H., Fairbairn, A. F., Jabeen, S., & Perry, E. K. (1992). Operational criteria for senile dementia of Lewy body type (SDLT). *Psychological Medicine, 22*, 911-922.

McKelvie, S. J. (1995). Vividness of Visual Imagery: Measurement, Nature, Function and Dynamics. *Journal of Mental Imagery, 19*(3&4), 20.

Meadows, J. (1974). Disturbed perception of colours associated with localized cerebral lesions. *Brain, 97*, 615-632.

Meco, G., Bonifati, V., Cusimano, G., Fabrizio, E., & Vanacore, N. (1990). Hallucinations in Parkinson's disease: Neuropsychological study. *Ital. Journal of Neuroscience, 11*, 373-379.

Mehta, Z., & Newcombe, F. (1991). A role for the left hemisphere in spatial processing. *Cortex, 27*, 153-167.

Mehta, Z., Newcombe, F., & Damasio, H. (1987). A left hemisphere contribution to visiospatial processing. *Cortex, 23*, 447-461.

Mellers, J. D., Quinn, N. P., & Ron, M. A. (1995). Psychotic and depressive symptoms in Parkinson's disease: a study of the growth hormone response to apomorphine. *British Journal of Psychiatry, 167*, 522-526.

Mellet, E., Tzourio, N., Denis, M., & Mazoyer, B. (1995). A positron emission tomography study of visual and mental exploration. *Journal of cognitive Neuroscience, 7*(4), 433-445.

Micheal, C. R. (1978). Color vision mechanisms in monkey striate cortex: Simple cells wth dual opponent-color receptive fields. *Journal of Neurophysiology, 41*, 1233-1241.

Mignard, M., & Malpeli, J. (1991). Paths of information flow through visual cortex.

Science, 251, 1249-1251.

MIkaelian, H. H. (1975). Interocular generalization of orientaion specific color aftereffects. *Vision Research, 15*(6), 661-663.

Miller, T. C., & Crosby, T. W. (1979). Musical hallucinations in a deaf elderly patient. *Annals of Neurology, 5*, 301-302.

Milner, A. D., & Goodale, M. A. (1995). *Cognition and Reality*. San Francisco: W.H. Freeman.

Milner, A. D., Perret, D. I., Johnson, R. S., Benson, P. J., Jordan, T. R., Heeley, D. W., & et al. (1991). Perception and action in "visual form agnosia". *Brain, 114*(405-428).

Milner, B. (1968). Visual recognition and recall after right temporal lobe excision in man. *Neuropsychologia, 6*, 191-209.

Mintz, S., & Alpert, M. (1972). Imagery vividness, reality testing and schizophrenic hallucinations. *Journal of Abnormal Psychology, 19*, 310-316.

Mishkin, M., Ungerleider, L. G., & Macko, K. A. (1983). Object vision and spatial vision: Two cortical pathways. *Trends in Neuroscience, 6*, 414-417.

Morrison, A. P., & Haddock, G. (1997). Cognitive factors in source monitoring and auditory hallucinations. *Psychological Medicine, 27*, 669-679.

Moskovitz, C., Moses, H., & Klawans, H. L. (1978). Levodopa induced psychosis: A kindling phenomenon. *American Journal of Psychiatry, 135*(6), 669-675.

Mueser, K. T., Bellack, A. S., & Brady, E. U. (1990). Hallucinations in schizophrenia. *Acta Psychiatr Scand, 82*, 26-29.

Murch, G. M. (1976). Classical conditioning of the McCollough effect: temporal parameters *Vision Research*, 16(6), 615-619

Musser., W.S., & Akil, M. (1996) Clozapine as a treatment for psychosis in Parkinson's disease: a review. *J. Neuropsychiatry Clin Neurosci., 8*, 1-9

Nagano, O., Takauchi, S., Nishitani, H., & Miyoshi, K. (1986). Hallucinatory symptoms in Parkinson's disease treatment with anti-Parkinsonian drugs. *Clinical Neurology, 26*(464-470).

Neisser, U. (1976). *Cognition and Reality*. San Francisco. CA.: W.H. Freeman.

Nelson, H. E. (1981). *National Adult Reading Test (NART)*. Windsor, Berks: NFER-Nelson.

Ogawa, S., Lee, T., Kay, A. R., & Tank, D. W. (1990). Brain magnetic resonance imaging with constrast dependent on blood oxygenation. *Proc. Natl. Acad. Sci, 3*,

9868-9872.

Ornstein, R., Johnstone, J., Herron, J., & Swencionis, C. (1980). Differential right hemisphere engagement in visuospatial tasks. *Neuropsychologia, 18*(1), 49-64.

Orrison, W. W., Lewine, J. D., Sanders, J. A., Rael, J. R., Davis, L. E., & Baldwin, N. G. (1995). Clinical magnetic source imaging. *Radiology, 197*(SS), 370.

Pallis, C. A. (1955). Impaired identification of faces and places with agnosia for colours. Report of a case due to cerebral embolism. *Journal of Neurology, Neurosurgery and Psychiatry, 18*, 218-224.

Parkin, A. J., & Walter, B. M. (1992). Recollective experience, normal aging and frontal dysfunction. *Psychology and ageing, 7*(2), 290-298.

Parkinson, J. (1817). *An Essay on the Shaking Palsy*. London: Sherwood, Neely and Jones.

Pavio, A. (1971). *Imagery and verbal processes*. New York: Holt, Rinehart, and Winston.

Pavio, A. (1986). *Mental representations*. new York: Oxford University Press.

Pederzoli, M., Girotti, F., Scigliano, G., Aiello, G., Carella, F., & Careceni, T. (1983). L-Dopa long-term treatment in Parkinson's disease: age related side effects. *Neurology, 40*, 259-269.

Penfield, W., & Perot, P. (1963). The brain's record of auditory and visual experience. *Brain, 86*, 595-696.

Perani, D., Gilardi, M. C., Cappa, S. F., & Fazio, F. (1992). PET studies of cognitive functions: a review. *Journal Nucl. Bio. Med., 36*(4), 324-336.

Perky, C. W. (1910). An experimental study of imagination. *American Journal of Psychology, 21*(21), 422-452.

Perry, E. K., Curtis, M., Dick, D. J., Candy, J. M., Atack, J. R., & et al. (1985). Cholinergic correlates of cognitive impairment in Parkinson's disease: comparisons with Alzheimer's disease. *Journal of Neurology, Neurosurgery and Psychiatry, 48*, 413-421.

Perry, E. K., Kerwin, J., Perry, R. H., Irving, D., Blessed, G., & Fairburn, A. (1990). Cerebral cholinergic activity is related to the incidence of visual hallucinations in senile dementia of the Lewy body type. *Dementia, 1*, 2-4.

Phillipson, O. T., & Harris, J. P. (1985). Perceptual changes in schizophrenia: a questionnaire study. *Psychological Medicine, 15*, 859-866.

Pirenne, M. H., & Denton, E. J. (1952). Accuracy and sensitivity of the human eye. *Nature, 170*, 1039-1042.

Poline, J. B., & Mozoyer, B. M. (1993). Analysis of individual positron emission tomography activation maps by detection of high signal-to-noise ratio pixel clusters. *Journal of Cerebral Blood Flow and Metabolism, 13*(3), 425-437.

Posner, M. I. (1978). *Chronometric explorations of the mind.* Chicago: University of Chicago Press.

Posner, M. I., & Petersen, S. E. (1990). The attentional system of the human brain. *Annual Review of Neuroscience, 13*, 25-42.

Press, W. H., Teukolsky, S. A., Vetterling, W. T., & Flannery, B. P. (1992). *Numerical Recipes in C: The Art of Scientific Computing.* Cambridge U.K: Cambridge Unversity Press.

Pylyshyn, Z. (1981). The imagery debate: Analogue media versus tacit knowledge. *Psychological Review., 88*, 16-45.

Pylyshyn, Z. W. (1973). What the mind's eye tells the minds brain: A critique of mental imagery. *Psycholoical Bulletin, 80*, 1-24.

Rabe-Hesketh, S., Bullmore, E., & Brammer, M. J. (1997). Analysis of functional magnetic resonance images. *Stat.Methods Med. Res., 6*, 215-237.

Rabins, P. V. (1982). Psychopathology of Parkinson's disease. *Comp. Psychiatry, 23*, 421-429.

Rajaram, S. (1993). Remembering and knowing: two means of access to the personal past. *Memory and Cognition, 21*(1), 89-102.

Rankin, P. M., & O'Carroll, P. J. (1995). Reality discrimination, reality monitoring and disposition towards hallucinations. *British Journal of Clinical Psychology, 34*, 517-528.

Ransmayr, Schmidhuber, E. B., Karamat, E., Engler-Plorer, S., Poewe, W., & Leidlmair, K. (1987). Visuoperception and visuospatial and visuospatial performance in Parkinson's disease. *Journal of Neurology, 235*(2), 99-101.

Rapcsak, S. Z., Comer, J. F., & Rubens, A. B. (1993). Anomia for facial expressions-neuropsychological mechanisms and anatomical correlates. *Brain and Language, 22*(2), 213-229.

Ratcliff, G. (1979). Spatial thought, mental rotation and the right cerebral hemisphere. *Neuropsychologia, 17*, 49-54.

Ratcliff, G., & Davis-Jones, G. A. B. (1972). Defective visual localization in focal brain wounds. *Brain, 95*, 49-60.

Reed, S. K. (1974). Structural descriptions and the limitations of visual images. *Memory and Cognition, 2*(2), 329-336.

Riddoch, M. J. (1990). Loss of visual imagery: A generation deficit. *Cognitive Neuropsychology, 7(4)*, 249-273.

Riddoch, M.J., & Humphreys, G.W. (1987) A case of integrative agnosia. *Brain 110(6)* 1431-1462

Riggs, L. A., White, K. D., & Eimas, P. D. (1974). Establishment and decay of orientation-contingent aftereffects of color. *Perception and Psychophysics, 16*(3), 535-542.

Rizzo, M., Smith, V., Pokorny, J., & Damasio, A. R. (1993). Color perception profiles in central achromatopsia. *Neurology, 43*(5), 995-1001.

Roland, P. E., & Gulyas, B. (1994). Visual imagery and visual representation. *Trends in Neuroscience, 17(7)*, 281-286.

Roland, P. E., & Gulyas, B. (1995). Visual memory, visual imagery, and visual recognition of large field patterns by human brain: Functional anatomy by positiron emission tomography. *Cerebral Cortex, 1*, 79-93.

Roland, P. E., & Gulyas, B. (1994). Visual representations of scenes and objects: retinotopical or non-retinotopical ? *Trends in Neuroscience, 17(7)*, 294-299.

Rondat, P., De Recondo, J., Coignet, A., & Ziegler, M., (1984) Mental disorders in Parkinson's disease after treatment with L-Dopa. *Adv Neurol* 40, 259-269

Roy, F. H. (1993). Occular Differential Diagnosis, 5th edition . Philadelphia: Lea & Faber.

Rubin, E. (1992). Delusions as part of Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioural Neurology, 5*, 108-113.

Sagar, H. J., Cohen, N. J., Sullivan, E. V., Corkin, S., & Growdon, J. H. (1988). Remote memory function in Alzheimer's disease and Parkinson's disease. *Brain, 111*, 185-206.

Sakai, K., Watanabe, E., Onodera, Y., Uchida, I., Kato, K., & Yamamoto, E. (1995). Functional mapping of the human colour centre with echo-planar magnetic resonance imaging. *Proc. R.Soc. Lond. B., 261*, 89-98.

Sanchez-Ramos, J. R., Ortoll, R., & Paulson, G. W. (1996). Visual hallucinations associated with Parkinson's disease. *Arch Neurol, 53*(1265-1268).

Sarbin, T. R. (1967). The concept of hallucination. *Journal of Personality, 35*, 359-380.

Savoy, R. L. (1984). "Extinction" of the McCollough effect does not transfer interocularly. *Perception and Psychophysics, 36*(6), 572-576.

Savoy, R. L., & Gabrielli, J. D. E. (1991). Normal McCollough effect in Alzheimer's disease and global amnesia. *Perception and Psychophysics, 9*(5), 448-455.

Schneider, G. E. (1969). Two visual systems. *Science, 163*, 895-902.

Segal, S. J. (1970). Imaging and reality: Can they be distinguished? In W. Keup (Ed.), *Origins and Mechanisms of Hallucinations* . New York: Plenum Press.

Segal, S. J., & Nathan, S. (1964). The Perky effect: Incorporation of an external stimulus into an imagery experience under placebo and control conditions. *Perceptual and Motor Skills, 18*, 385-395.

Seidenberg, M. S., & McClelland, J. L. (1989). A distributed, developmental model of word recognition and naming. *Psychological Review, 96*(4), 523-568.

Sereno, M. I., Dale, A. M., Reppas, J. B., Kwong, K. K., Beliveau, J. W., Brady, T. J., Rosen, B. R., & Tootell, R. B. H. (1995). Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Sceince, 268*, 889-893.

Servos, P., & Goodale, M. A. (1995). Preserved visual imagery in visual form agnosia. *Neuropsychologia, 33(11)*, 1383-1394.

Shepard, R. N., & Cooper, L. A. (1982). *Mental images and their transformations*. Cambridge, Mass.: MIT Press.

Shepard, R. N., & Metzler, J. (1971). Mental rotation of three-dimentional objects. *Science, 171*, 701-703.

Shuren, J. E., Brott, T. G., Schefft, B. K., & Houston, W. (1996). Preserved colour imagery in an achromatopic. *Neuropsychologia, 34*, 485-489.

Sietz, P. F., & Malholm, H. B. (1947). Relation of mental imagery to hallucinations. *Archieves of Neurology and Psychiatry, 57*, 469-480.

Simmons, A., Moore, E., & Williams, S. C. R. (1997). Automated quality control for FMRI studies. *Neuroimage, 5*(4), S466.

Skowbo, D., Timney, B. N., Gentry, T. A., & Morant, R. B. (1975). McCollough effects: Experimental findings and theoretical accounts. *Psychological Bulletin, 82*, 497-510.

Slade, P. D. (1976). An investigation of psychological factors involved in the predisposition to auditory hallucinations. *Psychological Medicine, 6*, 123-132.

Snodgrass, J. G., & Vanderwart, M. (1980). A standardized set of 260 Pictures: Norms

for name agreement , familiarity, and visual complexity. *Journal of Experimental Psychology: Human Learning and Memory, 6*(2), 174-215.

Stacy, M., & Jankovic, J. (1992). Clinical and neurobiological aspects of Parkinson's disease. In S. J. Huber & J. L. Cumming (Eds.), *Parkinson's Disease: Neurobiological Aspects* . New York: Oxford University Press.

Starker, S., & Jolin, A. (1982). Imagery and hallucinations in schizophrenic patients. *Journal of Mental Disorders, 170*, 448-451.

Starkstein, S., Robinson, R., & Berthier, M. (1992). Post-stroke hallucinatory delusional syndromes. *Neuropsychiatry, Neuropsychology and Behavioural Neurology, 5*, 114-118.

Steckler, T., & Sahgal, A. (1995). The role of serotonergic-cholinergic interactions in the mediation of cognitive behaviour. *Behav. Brain Rev.*, 165-199.

Stehling, M. K., Turner, R., & Mansfield, P. (1991). Echo-planar imaging: magnetic resonance imaging in a fraction of a second. *Science, 254*(5028), 43-50.

Stengel, E. (1948). The syndrome of visual alexia with colour agnosia. *Journal of Mental Science, 94*, 46-58.

Sternberg, S. (1969). The discovery of processing stages: Extensions of Donders' method. *Acta Psychologica, 30*, 276-315.

Stromeyer, C. F. (1972). Edge-contingent color aftereffects: Spatial frequency specificity. *Vision Research, 12*, 717-733.

Stromeyer, C. F., & Dawson, B. M. (1978). Form colour aftereffects: Selectivity to local luminance constrast. *Perception, 7*(4), 407-415.

Sweet, R. D., McDowell, F. H., Feigenson, J. S., Loranger, A. W., & Goodell, H. (1976). Mental symptoms in Parkinson's disease during chronic treatment with Levodopa. *Neurology, 1976*(26), 305-310.

Symonds, C., & MacKenzie, I. (1975). Bilateral loss of vision from cerebral infarction. *Brain, 80*, 28-48.

Tagaris, G. A., Kim, S. G., Strupp, J. P., Andersen, P., Ugurbil, K., & Georgopoulus, A. P. (1996). Quantitative relations between parietal activation and performance in mental rotation. *Psychophysiology, 35*, 151-161.

Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain.* New York: Theme.

Tanaka, K., & Saito, H. (1989). Analysis of motion of the visual field by direction,

expansion/contraction and rotational cells clustered in the dorsal part of the medial superior temporal area of the macaque monkey. *Journal of Neurophysiology, 62*, 626-641.

Tanner, C. M., Vogel, C., Goetz, C. G., & et al. (1983). Hallucinations in Parkinson's disease: a population study. *Ann. Neurol., 14*(1), 136.

Taylor, A., & Warrington, E. K. (1971). Visual agnosia: A single case report. *Cortex, 7*(2), 152-161.

Taylor, A. E., Saintcyr, J. A., & Lang, A. E. (1976). Frontal-lobe dysfunction in Parkinson's disease: The cortical focus of neostriatal outflow. *Brain, 109*(5), 845-883.

Teft, L. W., & Clark, F. T. (1968). The effects of stimulus density on orientation specific aftereffects of colour adaptation. *Psychonomic Science, 11*(8), 265-266.

Thurstone, T. G. (1958). *Manual for SRA primary mental abilities*. Chicago: Sc.Res.Ass.

Tison, F., Dartigues, J. F., Auriacombe, S., & Letenneur, L. (1995). Dementia in Parkinson's disease: A population based study in ambulatory and institutionalized individuals. *Neurology, 45*(5), 705-708.

Todes, C.J.& Lees (1985) The pre-morbid personality of patients with Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry, 48,* 97-100

Tootell, R. B., & Hadjikhani, H. K. (1998). Has a new color area been discovered? [letter reply]. *Nature Neuroscience, 1*(5), 335-336.

Tootell, R. B. H., Reppas, J. B., Dale, A. M., Look, R. B., Serano, M. I., Malach, R., Brady, T. J., & Rosen, B. R. (1995). Visual motion aftereffect in human cortical area MT revealed by functional magnetic resonance imaging. *Nature, 375*, 139-141.

Trimble, M. (1992). The schizophrenia-like psychosis of epilepsy. *Neuropsychiatry, Neuropsychology and Behavioral Neurology, 5*, 103-107.

Tulving, E. (1983). *Elements of Episodic Memory*. Oxford: Oxford Science.

Tulving, E. (1985). Memory and consciousness. *Canadian Psychologist, 26*, 1-12.

Tulving, E., Kapur, S., Markowitsch, H. J., Craik, F. I. M., Habib, M., & Houles, S. (1994). Neuroanatomical correlates of retrieval episodic memory: Auditory sentence recognition. *Proc. Nat. Acad. Sci. USA, 91*, 2012-2015.

Van Essen, D. C. (1985). Functional organisation of primate visual cortex. In A. Peters & E. G. Jones (Eds.), *Cerebral Cortex* (Vol. 3, pp. 259-329). New York: Plenum.

Vidyasagar. (1976). Orientation specific colour adaptation at a binocular site. *Nature, 261*, 39-40.

Vinogradov, S., Willis-Shore, J., Poole, J. H., Marten, E., & Ober, B. (1997). Clinical and neurocognitive aspects of source monitoring errors in schizophrenia. *American Journal of Psychiatry, 154*(11), 1530-1537.

Walter, H., Podreka, I., Steiner, M., Suess, E., & et al. (1990). A contribution to classification of hallucinations. *Psychopathlogy, 23*(2), 97-105.

Warrington, E. K. (1984). *Recognition Memory Test*. Windsor: Nelson.

Warrrington, E. K., & James, M. (1991). *The Visual Object and Space Perception Battery Test*. Bury St Edmunds: Thmaes Valley Test Company.

Watkin, M. J., & Schiano, D. J. (1982). Chromatic imaging- An effect of mental coloring on recognition memory. *Cand. J. Psychol., 36*(2), 291-299.

Watson, J. (1913). Psychology as the behaviourist views it. *Psychological Review, 20*(2), 158-177.

Watson, J. D. G., Myers, R., Frackowiak, R. S. J., Hajnal, J. V., Woods, R. P., Mazziota, J. C., Shipp, S., & Zeki, S. (1993). Area V5 of the human brain: Evidence from a combined study using positron emission tomography and magnetic resonance imaging. *Cerebral Cortex, 3*, 79-94.

Weinberger, L. M., & Grant, F. C. (1940). Visual hallucinations and their neuro-optical correlates. *Arch. Ophthalmol., 23*(169-199).

West, L.J., (1962) A general theory of hallucinations and dreams. In L.J.West (Ed), *Hallucinations* (pp 275-291). New York: Grune & Stratton

White, K. D., & Riggs, L. A. (1974). Angle contingent color aftereffects. *Vision Research, 14*(11), 1147-1154.

White, N. J. (1980). Complex visual hallucinations in partial blindness due to eye disease. *British Journal of Psychiatry, 136*, 284-286.

Wild, H. M., Butler, S. R., Carden, D., & Kulikowski, J. J. (1985). Primate cortical area V4 important for colour constancy but not wavelength discrimination. *Nature, 313*, 133-135.

Wippich, W. (1992). Implicit and explicit memory without awareness. *Psychological Research, 54*(3), 212-224.

Wittgenstein, L. (1953). *Philosophical investigations*. New York: Macmillian.

Wolters, E.C., Jansen, E.N.H., Tuynman-Qua, H.G., & Bergmans, P.L.M. (1996) Olanzapine in the treatment of dopaminomimmetic psychosis in patients with Parkinson's disease. *Neurology ,47,* 1085-1087

Young, A. B., & Penney, J. B. (1993). Biochemical and functional organisation of the basal ganglia. In J. Jankovic & E. Tolosa (Eds.), *Parkinson's Disease and Movement Disorders 2nd ed.* Baltimore: Williams & Wilkins.

Yuille, J. C., & Steiger, J. H. (1982). Nonholistic processing in mental rotation. *Perception and Psychophysics, 34,* 265-169.

Zeki, S. (1993a). *A vision of the brain.* Oxford: Blackwell.

Zeki, S. (1973). Colour coding in the rhesus monkey prestriate cortex. *Brain Res., 27,* 422-427.

Zeki, S. (1991b). Cerebral Akinetopsia. *Brain, 114,* 811-824.

Zeki, S., & Marini, L. (1998). Three cortical stages of colour processing in the human brain. *Brain, 121,* 1669-1685.

Zeki, S., Watson, J., & Frackowiack, R. (1993b). Going beyond the information given: the relation of illusory visual motion to brain activity. *Proceedings Of The Royal Society of London.B., 252,* 215-222.

Zeki, S., Watson, J. D. G., Lueck, C. J., Kennard, C., & Frackowiak, R. S. J. (1991a). A direct demonstration of functional specialization in human visual cortex. *The Journal of Neuroscience, 11(3),* 641-649.

Zeki, S. M. (1983). The distribution of wavelenght and orientation selective cells in different areas of monkey visual cortex. *Proc. Royal. Soc. Lond. Bio Sci., 217,* 449-470.

Zeki, S. M. (1977). Color coding in the superior temporal sulcus of the rhesus monkey visual cortex. *Proc. R. Soc. Lond. B. Biol. Sci., 197*(1127), 195-223.

Zeki, S. M. (1990). A century of cerebral achromatopsia. *Brain, 113,* 1721-1777.

Zeki, S. M., McKeefry, D. J., Bartel, A., & Frackowiak, R. S. (1998). Has a new color area been discovered [letter]. *Nature Neuroscience, 1*(5), 335-336.

Zeki, S. M., & Shipp, S. (1988). The functional logic of cortical connections. *Nature, 335,* 311-317.

Zihl, D., Von Camon, D., & Mai, N. (1983). Selective disturbance of movement vision after bilateral brain damage. *Journal of Experimental Psychology: Learning, memory and cognition, 331,* 679-684.

Appendix A1

Pre-recorded questions for colour imagery experiment (phase A)

Is a raspberry darker red than a strawberry?

Is pine darker green than grass?

Is the sea darker blue than the sky?

Are canaries darker yellow than lemons?

Are London buses darker red than post-boxes?

Are daffodils darker yellow than dandelions?

Are peas darker green than broccoli?

Are baked beans darker orange than carrots?

Is the cover of yellow pages darker yellow than a banana?

Are walnuts darker brown than brazil nuts?

Is a fox darker brown than a mouse?

Is the outside of a cucumber darker green than the inside?

Is a sparrow darker brown than a thrush?

Is orange peel darker orange than the fruit inside?

Are apples darker red than peaches?

Is an avocado darker green than asparagus?

Is the light on a police car darker blue than police uniform?

Is the blue on the Union Jack darker than that on the Stars and Stripes?

Is the green of an emerald darker than that of a pea?

Is the orange of autumnal leaves darker than a carrot?

Is the yellow of egg yolk darker than daffodils?

Is oak wood darker brown than pine?

Is honey darker brown than sand?

Are blackourrants darker purple than blueberries?

Are pigs darker pink than people?

Are gold coins darker gold than gold rings?

Are bricks darker red than blood?

Is strawberry icecream darker pink than carnations?

Are lemons darker yellow than bananas?

Are courgettes darker green than grass?

Are tigers darker orange than carrots?

Appendix A2

Pre-recorded questions for colour imagery experiment (phase B)

IS THE ANGLE BETWEEN THE MINUTE AND HOUR HAND ON A CLOCK GREATER THAN OR EQUAL TO 90 DEGREES WHEN:
The time on the clock is:

10 to 3?
5 past 10?
Half past 4?
20 past 6?
5 to 7?
20 past 3?
Half past 5?
10 to 7?
5 past 2?
10 o'clock?
Quarter past 3?
5 to 9?
25 past 6?
10 past 11?
quarter to 8?
10 to 10?
half past 2?
5 past 6?
5 to 2?
20 past 11?
10 to 6?
20 to 3?
5 past 7?
10 past 3?
half past 1?
2 o'clock?
20 past 7?
quarter to 8?
10 to 4?
5 past 9?

Name

1. MMSE.....

2. NART.....

3. The VOSP:

Incomplete letters (20) .....

Silhouettes

Objects (15).....

Animals (15).....

Object Decision (20).....

P. Silhouettes 2 x (10).....

Dot Counting (10).....

Cube Analysis (20).....

Position Discrimination (20).....

Number Location (10).....

4. Warrington

Words.....

Faces.....

5. Verbal Fluency,

F.....

A.....

S.....

Total.....

6. Imagery Questionnaires

Shapes (10).....

Letters (10).....

Mental Hue Comparison.....

7. Semanic

Living Visual (10).....

Living Non-visual (10).....

Non-living Visual (10).....

Non-living Non-visual (10).....

8. VVIQ.....

N	NVH	VH

8 Source Monitoring

Encoding Set A B

Retrieval Set A B

Number if items recognised:

Retrieval

Encoding	*Words*	*Pictures*
Words		
Pictures		

No. of false positves.....

Number of items correctly allocated to source:

Retrieval

Encoding	***Words***	***Pictures***
Words		
Pictures		

R and K

Retrieval

Encoding	*Words*		*Pictures*	
	R	*K*	*R*	*K*
Words				
Pictures				

False Rs.....

False Ks.....

P D Q - 1

VISION QUESTIONNAIRE

**Department of Psychology,
The University of Reading,
Whiteknights,
Reading RG6 6AL**

We are studying possible visual changes in normal ageing and in Parkinson's disease. In order to carry out this study, we need to obtain information from people who do not have Parkinson's disease as well as from people who do. As part of this study, we are carrying out a questionnaire survey, and would like to ask you to help us by completing this form (which should take about fifteen minutes of your time). You are under no obligation to do so, but your help would be much appreciated.

Dr Alison Lee
Tel: 0118 9318522

Dr John Harris
Tel: 0118 9318522

Changes in Vision Questionnaire

This questionnaire concerns possible changes in how things look, changes in carrying out some everyday tasks, and changes in the occurrence of certain visual symptoms, which you may have noticed in the last few years. Please think carefully before answering each question but do not spend too much time on each one.

The chief aim of the questionnaire is to find out whether sufferers from Parkinson's disease have experienced visual changes. However, even if you are not a sufferer, please take the time to complete the questionnaire: we need to know whether changes in seeing or the other tasks may occur as part of normal ageing, or in connection with another illness, in order to understand possible effects of Parkinson's disease.

All information will be treated in strictest confidence, and you are not required to give your name unless you wish. Thank you very much for taking time to answer this questionnaire.

It would be helpful if you would complete the questionnaire using a soft pencil, and use an eraser when making any changes

Section One: This section asks about some personal details.

1. How old are you ? Please give your age in years - one number in each box, e.g. ☐7☐3 ☐☐☐

Where necessary, please put a cross in the appropriate box, e.g. ☒.

2. Are you male or female? Male ☐ Female ☐

3. Are you right- or left-handed ? Please choose one box below:

Strongly right-handed	Weakly right-handed	Ambidextrous	Weakly left-handed	Strongly left-handed
☐	☐	☐	☐	☐

4. Do you suffer from any long-term illness? Yes ☐ No ☐

(e.g. Parkinson's disease, diabetes etc.)

If yes, please state which, and approximately when this was diagnosed (if you suffer from more than one, please state all)

Illness	Year diagnosed

5. Are you taking any medication at the moment? Yes ☐ No ☐

If yes, please state the drug(s) and the dose you take each day. (Please include all medication even if it has nothing to do with Parkinson's disease, and continue on the back of this page if necessary)

Name of drug	Dose taken

6. When did you last see a consultant neurologist? _____

7. Do you experience tremor in any of your limbs? Yes ☐ No ☐

If you do experience tremor, please rate its severity on the scale below, where 1 is 'very mild' and 5 is 'very severe' tremor.

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

If you do experience tremor, does it get better after medication? Yes ☐ No ☐

Please rate any improvement on the scale below, where 1 is 'very small' and 5 is 'very pronounced' improvement

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

8. Do any of your limbs feel rigid? Yes ☐ No ☐

If you do experience any rigidity, please rate it on the scale below, where 1 is 'very mild' and 5 is 'very severe' rigidity

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

If you do experience any rigidity, does it ease after medication? Yes ☐ No ☐

Please rate any improvement on the scale below, where 1 is 'very small" and 5 is 'very pronounced' improvement

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

9. Do you have problems in starting to move? Yes ☐ No ☐

Please rate any problems in starting to move on the scale below, where 1 is 'very mild' and 5 is 'very severe'

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

If you have problems in starting to move, is movement easier after medication? Yes ☐ No ☐

Please rate any improvement on the scale below, where 1 is 'very small' and 5 is 'very pronounced' improvement

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

10. Do you ever 'freeze' and find it difficult to start moving again? Yes ☐ No ☐

If you do 'freeze', please rate the extent of this problem on the scale below, where 1 is 'very mild' and 5 is 'very severe'

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

If you do 'freeze', does freezing decrease after medication? Yes ☐ No ☐

Please rate any improvement on the scale below, where 1 is 'very small' and 5 is 'very pronounced' improvement

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

11. If you experience any of the previous symptoms, which do you find most impairing?

Tremor ☐ Rigidity ☐

Starting to move ☐ Freezing ☐

12. Which do you find most distressing?

Tremor ☐ Rigidity ☐

Starting to move ☐ Freezing ☐

13. Are your symptoms only on one side? Yes ☐ No ☐

If so, which side? Left ☐ Right ☐

14. Do you think your symptoms are disabling ? Often ☐ Sometimes ☐ Never ☐

15. Are your posture and gait affected?

Often	Sometimes	Never
☐	☐	☐

16. Do you have problems in standing up?

Often	Sometimes	Never
☐	☐	☐

17. Can you still get around the home unassisted (without help from others or a wheelchair) ?

Usually	Sometimes	Never
	☐	☐

18. Have you ever consulted a doctor about a problem at the front of the eye, e.g., cataract ?

Yes	No
☐	☐

19. Do you have fainting attacks?

Often	Sometimes	Never
☐	☐	☐

20. Do you suffer from motion sickness? (when you travel in cars, planes etc.)

Often	Sometimes	Never
☐	☐	☐

Section Two: This section asks questions about vision or tasks in which vision may be important.

21. Do familiar things around you ever appear to have changed their appearance unnaturally in some way ?

Yes	No
☐	☐

If Yes, how often does this happen?

More than 5 times per week	1-5 times per week	less than once per week
☐	☐	☐

22. Do you ever see things that are not really there ?

Yes	No
☐	☐

If Yes, how often does this happen?

More than 5 times per week	1-5 times per week	less than once per week
☐	☐	☐

If you answered YES, to Question 21 or Question 22 (or both), please answer Questions 23-27. Otherwise, please go on to Question 28.

PDQ-6

23. Do the things you see have particular form ? (e.g. people, objects, animals, shapes, etc.) Yes ☐ No ☐

If yes, please describe what you see in detail.

24. How long do the images appear for ? Hours ☐ Mins ☐ Secs ☐

25. Do the images move ? Yes ☐ No ☐

26. Do the images appear:

when you wake up ☐ when you go to sleep ☐ morning ☐ afternoon ☐ evening ☐ ? (tick more than one if necessary)

27. Do you think that it is your medication which causes the images ? Yes ☐ No ☐

28. Can you still do the following everyday tasks with the same ease as you used to ?

Task	Yes	No	If no, reason/possible explanation
Reading	☐	☐	
Writing	☐	☐	
Watch TV	☐	☐	
Knitting/ Sewing	☐	☐	
Jigsaws	☐	☐	
Cross-word puzzles	☐	☐	

Are there any other tasks you feel have been affected? In what ways?

Department of Psychology, The University of Reading

29. Do vehicles or people on the street ever appear to move unnaturally? Often ☐ Sometimes ☐ Never ☐

If they appear changed, does the movement seem:

Slower ☐ More jerky ☐ Smoother ☐ Faster ☐

Other - please describe:

30. Have you ever suffered from 'freezing' episodes when trying to walk through narrow spaces, such as doorways?

Yes ☐ No ☐

If so, have you ever tried any of the following tricks to help you get going again ?

Trick	Yes	No	If yes, did it work ? Any comments ?
Dropping then stepping on a target, such as a piece of paper or cloth	☐	☐	
Closing your eyes	☐	☐	
Reaching out to touch the sides before continuing	☐	☐	
Taking longer strides	☐	☐	
Taking a step backwards	☐	☐	

Are there any other tricks which you use that you feel may be of use to others? If so, could you describe them?:

31. Do you find that you bump into the sides of doorways or other objects such as furniture as you move around a building ?

Often	Sometimes	Never
☐	☐	☐

If you do bump into the sides of doorways or furniture, are these usually ?

On your left side	On your right side	Equally often left and right
☐	☐	☐

32. We are always looking for sufferers from Parkinson's disease who might be willing to visit Reading to take part in tests of vision and so help us to understand the illness better. In addition, we have begun a study with Professor AS David and Mr Jim Barnes of Kings College Hospital, London, who are also interested in visual changes in the illness. Would you be interested in taking part in further research, either at Reading, or in London ? (Your travelling expenses would be paid, and you would be free to withdraw from the studies at any time). If you leave a contact address and/or telephone number in the space below, we will give you more information about the studies we are carrying out, and/or put you in touch with Professor David or Mr Barnes. It would be perfectly in order to decline to take part, once you had been given details.

If you are interested in taking part in further research, please leave a contact name and address, and/or telephone number below:

Thank you very much for taking time to complete this questionnaire.

Could you please return this questionnaire in the envelope to Dr Alison Lee, Department of Psychology, The University of Reading, Whiteknights, Reading RG6 6AL.

Appendix B2

Visual Changes in Parkinson's Disease Questionnaire

We are studying the neurological and psychological processes underlying visual disturbances (VDs) in patients with Parkinson's disease (PD). This will be achieved by carrying out detailed neuropsychological tests on PD patients with a history of prominent VDs in comparison to a matched group without such a history. VDs can be extremely distressing; they are frequently under-reported and sometimes inadequately treated. Understanding some of the basic mechanisms underlying in PD would not only inform treatment strategies but would improve our understanding of perceptual aberrations in general.

The initial part of this study is a questionnaire survey, and we would like to ask you to help us by completing this form (which should take about fifteen minutes of your time). You are under no obligation to do so, but your help would be much appreciated. In order to carry out this study, we need to obtain information from people who do not have visual changes as well as from people who do, so even if you are not a sufferer, please take the time to complete the questionnaire.

All the information will be treated in strictest confidence. Thank you very much for taking time to answer this questionnaire.

Section One

This section asks about personal details

Name.....

1. How old are you? ☐☐

2. Are you Male or female? Male ☐ Female ☐

3. Are you taking any medication at present? Yes ☐ No ☐

If yes, please state the drug(s) and the dose you take each day

4. How long have you suffered from Parkinson's Disease?

5. Do you suffer from any other long-term illness? Yes ☐ No ☐

If yes, please state which one and approximately when it was diagnosed.

6. Are your symptoms of PD on one side? Yes ☐ No ☐

If so which side? Left ☐ Right ☐

7. Do you suffer from migraine? Yes ☐ No ☐

8. Can you still get around the house unassisted (without help from other or a wheelchair)

Yes ☐ No ☐

9. Have you ever consulted a doctor about a eye problem? Yes ☐ No ☐

If yes, please give details

Section 2

This section asks questions about vision

10. Do familiar things around you ever appear to change their appearance unnaturally in some way? Yes ☐ No ☐

If yes, now often does this happen

More than 5 times a week ☐ 1-5 times a week ☐ less than once a week ☐

11. Do you see things that are not really there Yes ☐ No ☐

If yes, now often does this happen

More than 5 times a week ☐ 1-5 times a week ☐ less than once a week ☐

If you answered Yes to Question 10 or 11 (or both), please answer the questions in section 3.

Section 3

This section asks questions about your visual disturbances

12. Do these things you see have particular forms ?
(eg, people, objects, animals, shapes etc) Yes ☐ No ☐

If yes please give details

13. Do these visual images come on suddenly Yes ☐ No ☐

14 How long do the images appear for? Hours ☐ Mins ☐ Secs. ☐

15. Do these images move? Yes ☐ No ☐

16. Do the images appear:

when you wake up ☐ when you go to sleep ☐ morning ☐ afternoon ☐ evening ☐

(tick more than one if necessary)

17. How many images appear? One ☐ 2-5 ☐ >5 ☐

18. What is the clarity of these images? Sharp ☐ Blurry ☐ Transparent ☐ Variable ☐

19. Do you have control over these images? Yes ☐ No ☐
(eg Can you make them appear/disappear?)

20. What is the colour of these images?

Black & White ☐ Single colour ☐ Multiple colours ☐

21. Do the images have movement?

Move ☐ Don't move ☐

22. When these images appear are your eyes open or closed?

Open ☐ Closed ☐ Either ☐

23. How do these image appear to you?

Real ☐ Unreal ☐ Not sure ☐

24. What is the ambient light when these image appear?

Bright ☐ Dim ☐ Dark ☐

25. Do these image start with a real perception?
(eg When you are looking at a object or person)

Yes ☐ No ☐

26. Do you think that it is your medication which causes the images?

Yes ☐ No ☐

27. What is the content of the images?

Stereotyped ☐ Different ☐

Please give details

28. Do these images occupy your field of vision?

Completely ☐ Partially ☐

29 Are the image distorted in some way?

Yes ☐ No ☐

If yes please give details

Thank you for answering this questionnaire

Appendix B3: Imagery Questionnaires

Shape Attributes

Answer whether these statements about shapes of the following objects are true or false.

1. A drum is shaped like a cylinder.	True
2. A sofa is taller than it is wide.	False
3. The body of a snake usually appears curved.	True
4. The body of a violin is square .	False
5. A table has a pointed top.	False
6. A cat has pointed ears.	True
7. The spokes of a wheel are curved.	False
8. A television has an oval screen	False
9. A bus is longer than it is wide.	True
10. A tent has a pointed top.	True
11. An apple is round.	True
12. A walnut is square.	False
13. A shoe is wider than it is long.	False
14. A brick is rectangular	True.

Letter Imagery

Name.....

Are the capital block form of these letters formed by straight lines (SL), curved lines (CL) or a combination of both (B) ?

1. Q	SL CL B
2. W	SL CL B
3. O	SL CL B
4. Z	SL CL B
5. P	SL CL B
6. U	SL CL B
7. C	SL CL B
8. M	SL CL B
9. R	SL CL B
10. S	SL CL B

Total /10

Living-Visual

Name.....

1. Does a fox have hooves ?	Yes / No
2. Does a giraffe have small horns ?	Yes / No
3. Is the body of a butterfly long and narrow ?	Yes / No
4. Does a donkey have a long tail ?	Yes / No
5. Are hedgehogs brown ?	Yes / No
6. Do parrots have feathered feet ?	Yes / No
7. Do bears have rounded ears ?	Yes / No
8. Is a toadstool smoother on the underside of its cap ?	Yes / No
9. Does a lizard have six legs ?	Yes / No
10.Are holly leaves shiny ?	Yes / No

Total /10

Living-Non visual

Name.....

1. Are frogs amphibians ?	Yes / No
2. Are squirrels farm animals ?	Yes / No
3. Are sheep domesticated for their meat ?	Yes / No
4. Is a crab a mammal ?	Yes / No
5. Are kangaroos native to Britain ?	Yes / No
6. Can tortoises live as long as humans ?	Yes / No
7. Do people ride camels	Yes / No
8. Are daffodils sought for their medical powers ?	Yes / No
9. Are toadstools a type of fungus ?	Yes / No
10. Do cats hatch from eggs ?	Yes / No

Total /10

Non living-Visual

Name.....

1. Are ladders stored on the outside of the fire engine ?	Yes / No
2. Is a electric drill shaped like a gun ?	Yes / No
3. Are wheelbarrows cylindrical ?	Yes / No
4. Is there a screw at the centre of a pair of scissors ?	Yes / No
5. Is a teacup taller than a mug ?	Yes / No
6. Is the head of a axe square in shape ?	Yes / No
7. Do tricycles have two wheels at the front and one at the back ?	Yes / No
8. Does a trumpet have keys on the top ?	Yes / No
9. Can a stool have three legs ?	Yes / No
10. Is a face cloth bigger than a hand towel ?	Yes / No

Total /10

Non living-Non visual

Name.....

1. Is a kettle used for baking ?	No
2. Were there cars in 1750 ?	No
3. Is it possible to drill through plaster ?	Yes
4. Are mops considered to be a gardening tool ?	No
5. Is a vice used for clamping objects together ?	Yes
6. Do you need a licence to drive a car ?	Yes
7. Are binoculars used at sporting events ?	Yes
8. Does sawdust result from sawing wood ?	Yes
9. Can a canoe go as fast as a speed boat ?	No
10. Does a thermometer measure wind speed?	No

Total /10

Appendix C1

Mini-Mental State Examination

ERROR	CORRECT	NOT ASSESSED	
0	1	9	1) What is the year? _____
0	1	9	2) What is the season of the year? _____
0	1	9	3) What is the date? _____
0	1	9	4) What is the day of the week? _____
0	1	9	5) What is the month? _____
0	1	9	6) Can you tell me where we are? _____ (For instance, what state are we in?)
0	1	9	7) What county are we in? _____
0	1	9	8) What city/town are we in? _____
0	1	9	9) What floor of the building are we on? _____
0	1	9	10) What is the name or address of this place? _____

"Now I would like to ask you some questions to check your memory and concentration. Some of them may be easy and some of them may be hard."

11) I am going to name three objects. After I have said them, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes.

Please repeat the names for me:
(Score first try. Repeat objects for three trials only.)

0	1	9 Apple
0	1	9 Table
0	1	9 Penny

12) Now I am going to give you a word and ask you to spell it forwards and backwards. The word is WORLD. First, can you spell it forwards? Now spell it backwards.

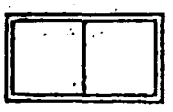
(Repeat if necessary, and help subject spell word forward, if necessary)

Score number of letters given in correct order ___ ___ ___ ___ ___

(0 to 5; 9 = not assessed)

Mini-Mental State Examination

ERROR	CORRECT	NOT ASSESSED	
			What were the three objects I asked you to remember?
0	1	9	13) Apple _____
0	1	9	14) Table _____
0	1	9	15) Penny _____
0	1	9	16) (Show wrist watch) What is this called? _____
0	1	9	17) (Show pencil) What is this called? _____
0	1	9	18) I would like you to repeat a phrase after me: (The phrase is) "NO IF'S, AND'S OR BUT'S" Allow only one trial.
0	1	9	19) Read the words on this page, then do what it says. (The paper reads) "CLOSE YOUR EYES" Code correct if subject closes eyes.
			20) I'm going to give you a piece of paper. When I do, take the paper in your right hand, fold the paper in half with both hands, and put the paper down on your lap.
0	1	9	Right hand
0	1	9	Folds
0	1	9	In lap
			Read full statement, THEN hand over paper. Do not repeat instructions or coach.
0	1	9	21) Write any complete sentence on that piece of paper for me.
0	1	9	22) Here is a drawing. Please copy the drawing on the same paper. Score correct if the two five-sided figures intersect to form a four-sided figure and if all angles in the five-sided figure are preserved.



TOTAL SCORE (The sum of the scores for all 22 questions, excluding any scores of '9')

Appendix C2

National Adult Reading Test (NART)

SECOND EDITION

Answer/Record Sheet

Name:..... Date of test:.....

	Errors		Errors
CHORD		SUPERFLUOUS	
ACHE		SIMILE	
DEPOT		BANAL	
AISLE		QUADRUPED	
BOUQUET		CELLIST	
PSALM		FACADE	
CAPON		ZEALOT	
DENY		DRACHM	
NAUSEA		AEON	
DEBT		PLACEBO	
COURTEOUS		ABSTEMIOUS	
RAREFY		DETENTE	
EQUIVOCAL		IDYLL	
NAIVE		PUERPERAL	
CATACOMB		AVER	
GAOLED		GAUCHE	
THYME		TOPIARY	
HEIR		LEVIATHAN	
RADIX		BEATIFY	
ASSIGNATE		PRELATE	
HIATUS		SIDEREAL	
SUBTLE		DEMESNE	
PROCREATE		SYNCOPE	
GIST		LABILE	
GOUGE		CAMPANILE	

Appendix C3

BECK INVENTORY

Name.....
Date.....

On this questionnaire are groups of statements. Please read each group of statements carefully. Then pick out the one statement in each group which best describes the way you have been feeling during the PAST WEEK INCLUDING TODAY. Circle the number beside the statement you picked. If several statements in the group seem to apply equally well, circle each one. Be sure to read all the statements in each group before making your choice.

1. 0 I do not feel sad
   1 I feel sad
   2 I am sad all the time and I can't snap out of it
   3 I am so sad or unhappy-that I can't stand it

2. 0 I am not particularly discouraged about the future
   1 I feel discouraged about the future
   2 I feel I have nothing to look forward to
   3 I feel that the future is hopeless and that things cannot improve

3. 0 I do not feel like a failure
   1 I feel I have failed more than the average person
   2 As I look back on my life, all I can see is a lot of failures
   3 I feel I am a complete failure as a person

4. 0 I get as much satisfaction out of things as I used to
   1 I don't enjoy things the way I used to
   2 I don't get real satisfaction out of anything anymore
   3 I am dissatisfied or bored with everything

5. 0 I don't feel particularly guilty
   1 I feel guilty a good part of the time
   2 I feel quite guilty most of the time
   3 I feel guilty all of the time

6. 0 I don't feel I am being punished
   1 I feel I may be punished
   2 I expect to be punished
   3 I feel I am being punished

7. 0 I don't feel disappointed in myself
   1 I am disappointed in myself
   2 I am disgusted with myself
   3 I hate myself

8. 0 I don't feel I am any worse than anybody else
   1 I am critical of myself for my weaknesses or mistakes
   2 I blame myself all the time for my faults
   3 I blame myself for everything bad that happens

9. 0 I don't have any thoughts of killing myself
   1 I have thoughts of killing myself, but I would not carry them out
   2 I would like to kill myself
   3 I would kill myself if I had the chance

10. 0 I don't cry any more than usual
    1 I cry more now than I used to
    2 I cry all the time now
    3 I used to be able to cry, but now I can't cry even though I want to

11. 0 I am no more irritated now than I ever am
    1 I get annoyed or irritated more easily than I used to
    2 I feel irritated all the time now
    3 I don't get irritated at all by the things that used to irritate me

12. 0 I have not lost interest in other people
    1 I am less interested in other people than I used to be
    2 I have lost most of my interest in other people
    3 I have lost all of my interest in other people

13. 0 I make decisions about as well as I ever could
    1 I put off making decisions more than I used to
    2 I have greater difficulty in making decisions than before
    3 I can't make decisions at all any more

14. 0 I don't feel I look any worse than I used to
    1 I am worried that I am looking old or unattractive
    2 I feel that there are permanent changes in my appearance
    3 I believe that I look ugly

15. 0 I can work about as well as before
    1 It takes an extra effort to get started at doing something
    2 I have to push myself very hard to do anything
    3 I can't do any work at all

16. 0 I can sleep as well as usual
    1 I don't sleep as well as I used to
    2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep
    3 I wake up several hours earlier than I used to and cannot get back to sleep

17. 0 I don't get more tired than usual
    1 I get tired more easily than I used to
    2 I get tired from doing almost anything
    3 I am too tired to do anything

18. 0 My appetite is no worse than usual
    1 My appetite is not as good as it used to be
    2 My appetite is much worse now
    3 I have no appetite at all anymore

19. 0 I haven't lost much weight, if any, lately
1 I have lost more than 5 pounds
2 I have lost more than 10 pounds
3 I have lost more than 15 pounds

I am purposely trying to lose weight by eating less
YES/NO

20. 0 I am no more worried about my health than usual
1 I am worried about physical problems such as aches and pains, or upset stomach, or constipation
2 I am very worried about physical problems and it's hard to think of much else
3 I am so worried about my physical problems that I cannot think about anything else

21. 0 I have not noticed any recent change in my interest in sex
1 I am less interested in sex than I used to be
2 I am much less interested in sex now
3 I have lost interest in sex completely

Appendix C4

Vividness of Visual Imagery Questionnaire

Name.....

Contact Phone No. / Email.....

Please consider carefully the following descriptions of pictures and rate the vividness of the image that comes before your mind's eye on a scale of 1-5 as indicated below

Ratings

1. Perfectly clear and as vivid as normal vision

2. Clear and reasonably vivid

3. Moderately clear and vivid

4. Vague and dim

5. No image at all, you only "know" that you are thinking of the object

Section A

Think of some relative or friend whom you frequently see (but who is not with you at present) and consider if you see before your mind's eye.....

1. The exact contour of face, head, shoulders and body. 1 2 3 4 5

2. Characteristic poses of head, attitudes of body etc. 1 2 3 4 5

3. The precise carriage, length of step, etc., in walking. 1 2 3 4 5

4. The different colours worn in some familiar clothes. 1 2 3 4 5

Section B

Visualize a rising sun. Consider if you see before your mind's eye.....

5. The sun rising above the horizon into a hazy sky. 1 2 3 4 5

6. The sky clearing and surrounding the sun in blueness. 1 2 3 4 5

7. Clouds. A storm blows up, with flashes of lightening. 1 2 3 4 5

8. A rainbow appearing. 1 2 3 4 5

Ratings

1. Perfectly clear and as vivid as normal vision

2. Clear and reasonably vivid

3. Moderately clear and vivid

4. Vague and dim

5. No image at all, you only "know" that you are thinking of the object

Section C

Think of the front of a shop which you often go to. Consider if you see before your mind's eye.....

9. The overall appearance of the shop from the opposite side of the road. 1 2 3 4 5

10 A window display including, shapes and details of individual items for sale. 1 2 3 4 5

11. The colour, shape and details of the door. 1 2 3 4 5

12. The counter assistant serving you and money changing hands 1 2 3 4 5

Section D

Think of a country scene which involves trees, mountains and a lake. Consider if you see before your minds eye....

13. The contours of the landscape. 1 2 3 4 5

14. The colour and shape of the trees. 1 2 3 4 5

15. The colour and shape of the lake. 1 2 3 4 5

16. A strong wind blowing in the trees and on the lake causing waves. 1 2 3 4 5

Thank you for answering these questions